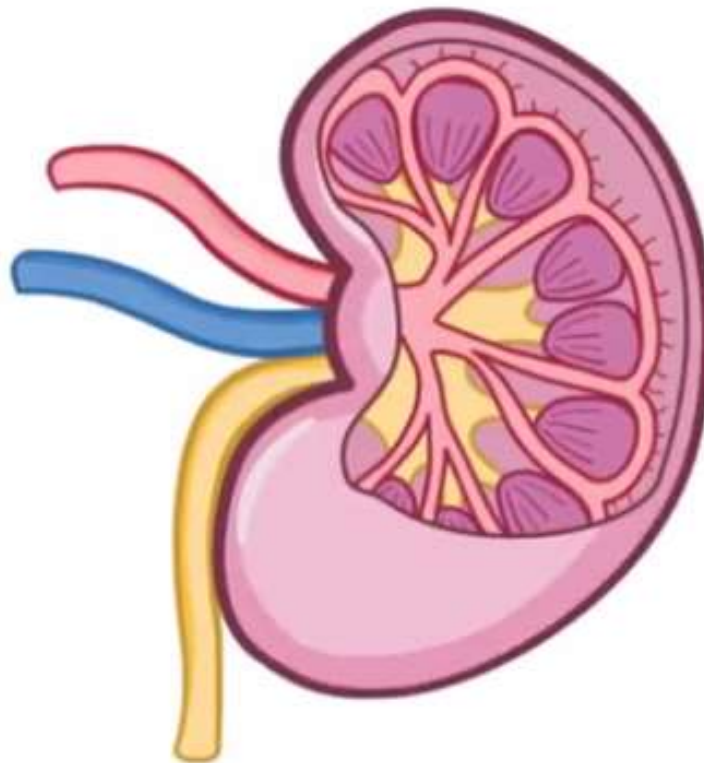

Nephrology

Written by:
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for
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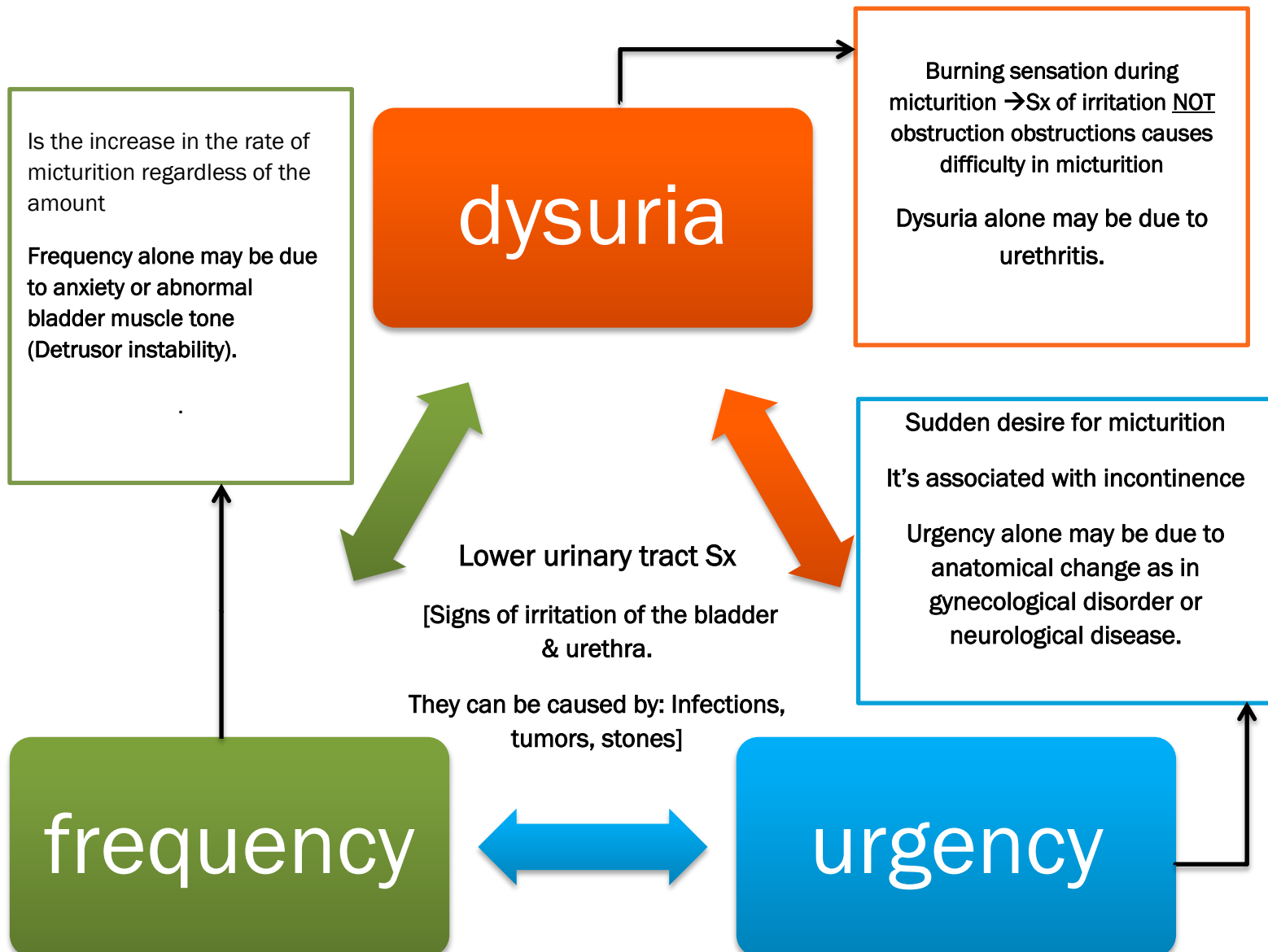
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Introduction Nephrology

1. Symptoms of Urinary System.
2. Investigations of Urinary System.
3. Renal Anatomy.
4. Renal Physiology.

Symptomology



Symptomology

Normal urine volume = 600 ml- 1800 ml / d.

Polyuria

Increase in urinary output > 3L/d regardless the frequency of micturition.

Causes

1. Diabetes mellitus
2. Diabetes Insipidus: Nephrogenic (Hypercalcemia, hypokalemia) or Neurogenic DI (more severe because it is not associated with polydipsia).
3. Diuretic therapy.
4. Psychogenic (polydipsia).
5. CKD (early).
6. Polyuric phase of acute tubular necrosis.

Severe polyuria will cause thirst, which may be the presenting symptom.

Oliguria and anuria

Oliguria: Urine output < 400 ml/day. Or < 0.5 ml /kg / hr.

400 ml/day is the minimal volume of urine which is necessary to excrete the waste products

Anuria: urine volume is < 100 ml / 24hrs,

- It raises the possibility of urinary tract obstruction!

Causes

1. Acute renal failure → AKI
 - Non oliguric renal failure is relatively common → 20% of cases (Frequently goes unrecognized).

Factors affect urine volume

1. Diet.
2. Physical activity and metabolic rate.
3. Renal function.

200 ml- 300 ml urine output / day might be sufficient for a healthy man on a protein free diet.

For example: 2L might be insufficient when chronic renal failure is present.

Factors affect urine volume

1. Diet.
2. Physical activity and metabolic rate.
3. Renal function.

200 - 300 ml / day as urine output might be sufficient for a healthy male on a protein free diet.

Whereas 2L might be insufficient if chronic renal failure is present.

Hematuria

Presence of blood in urine attributed to bleeding from the urinary tract

Painless	painful
Glomerulonephritis.	Urinary tract infections → M.C.C
UTI (tuberculosis and bilharziasis).	Renal stones.
Cancer bladder or papilloma. Hypernephroma.	Renal papillary necrosis.
Malignant hypertension.	
Renal cystic disease or renal vascular disease.	

- Hematuria+ Frequency or dysuria → usually bladder is the cause.
- Hematuria that clears during micturition → urethra.
- Hematuria all through → kidney.
- Terminal hematuria is also of bladder origin as in cases of bilharziasis

Pneumaturia

It means sensation of passing bubbles in the urine

This is usually caused by Vesicocolic fistula

? Chron's Disease
? Malignancy

Alteration of the force of micturition

A poor urinary stream is common in old males due to senile prostate.

- The force of the stream: Ask the patient to demonstrate how near he has to stand to an imaginary toilet.

May also occur with a urethral stricture (less common).

Other features of prostatic neck obstruction (Prostatism)

- Hesitancy: It is a delay in initiating urine flow. (may cause syncope)
- Urinary spray.
- post micturition dribbling
- Frequency.
- Nocturia.

Differential diagnosis of Nocturia:

Prostatic obstruction

Heart failure

Causes of polyuria

Obstructive Sleep

Apnea

Nocturia

The need to pass urine at night or during the sleeping hours may be a life-long habit.

Incontinence

It is inability of the urinary bladder to retain urine.

- Stress urinary incontinence: is provoked by the stress of laughing, sneezing or coughing, this is due to gynecological disorders.
- Retention with overflow leads to incontinence (neurogenic bladder).
- Urgency may also lead to incontinence (urge incontinence).

Some patients may have urge and stress incontinence at the same time.

Causes

Neurological	In males	In females
Spinal cord trauma or compression.	Benign prostatic hypertrophy prostatic carcinoma	Pelvic floor damage during childbirth in females.
Multiple sclerosis.	Incoordination of bladder sphincter function because of old age	Incoordination of bladder sphincter function because of old age

Urogenital pain

Renal pain

Is described as dull aching pain in the loin

The renal parenchyma is pain free and renal pain is associated with conditions causing stretching of the renal capsule and renal pelvis.

Causes

1. Hydronephrosis.
2. Stag horn stone.
3. Polycystic kidney (intermittent) due to spontaneous bleeding into a cyst.
4. Acute pyelonephritis.

Renal colic (Ureteric colic)

Usually due to ureteric obstruction by calculus or blood clot.

- It is a more severe pain due to obstruction of the ureter.
- The pain radiates downward to the groin and genitalia.
- Once a stone reaches the bladder, it becomes usually asymptomatic unless it enters the urethra to cause dysuria.
- The ureteric colic is usually severe and sustained associated with nausea and vomiting.

Investigations

Kidney function tests

1. Blood urea

Normally (20 -40 mg/dl)

The level of urea depends on the G.F.R & production rate of urea (Liver & protein intake)

- **Note:** a sudden increase in urea levels in CKD pt. could be due to Acute kidney injury on top of chronic kidney disease OR pt. had a high protein meal (not complying to dietary restrictions)

Increase production rate

1. Increased tissue catabolism and GIT bleeding.
2. Increased protein intake.
3. Sepsis
4. Tissue breakdown (provided that there is preexisting renal insufficiency).

Urea increases in sepsis by:

1. Increasing catabolism
2. Hypotension (septic shock)

Decreased production

1. chronic advanced liver disease
 2. reduced catabolism in old age
 - Example: Patient with the serum creatinine 10 mg/dl & mild urea you should consider liver disease.
- **Note:** urea levels may falsely low in pt. with advanced Chronic Liver Disease or SIADH.

2. Blood Urea Nitrogen (BUN)

Normally (10 -20 mg/dl)

It is similar to blood urea

Urea = BUN x 2

Septic shock by:

- Decrease total volume by either Hemorrhage or dehydration
- Vasodilation
- Stenosis before the kidney → Renal Artery Stenosis

3. Creatinine

Normally (0.7 - 1.4 mg/dl)

The level of the serum creatinine is less dependent on diet but is more related to the age, sex & muscular mass → creatinine may be found to be in the upper limit of normal in muscular athletes...

- Serum creatinine is a better guide to (GFR) than urea. It starts elevation when kidney Function (GFR) is reduced >70%.

4. B.U.N to Creatinine Ratio

Normally (10:1)

Causes of High B.U.N:Cr (PRERENAL/ GLOMERULAR)

Example: (BUN 200 , S.cr. 4 mg/dl)
ratio 50 : 1

Causes of Low B.U.N:Cr (TUBULAR CAUSES)

Example: (BUN = 60 , S.cr. 10 mg/dl)
ratio 6 : 1

High protein diet.	Associated liver disease.
GIT bleeding.	Acute tubular Necrosis.
Hyper-catabolic patient e.g. trauma, tissue breakdown	Hemodialysis patients - Urea is more dialyzable
Corticosteroid therapy.	Low protein diet
Pre renal failure	
Sepsis	

5. Creatinine Clearance

Normal Value (90-140 ml/ min for males, 80-125 ml/min for females)

It is the volume of plasma cleared from creatinine/min. It is a method to measure GFR *approximately*
 → it's usually slightly higher than the actual value

U = urine creatinine mg/dl.

V= volume of the urine per min.

P= plasma creatinine mg/dl.

$$\frac{U \times V}{P} \rightarrow V = \frac{\text{total urine volume in 24 hours}}{1440 \text{ (number of minutes in a day)}}$$

Serum creatinine starts elevation when creatinine clearance < 25%-30%.

GFR

The glomerular filtration rate (GFR) varies with age and sex but is approximately 120-130 ml/min/1.73 m² surface area.

It can be measured by renal scan using Diethylene Tri-amine Penta-Acetic acid labeled with Technetium (99mTc-DTPA).

It is more accurate than creatinine clearance.

GFR 35-50% → of normal is sufficient to maintain the patient symptom free.

GFR 20-35% → azotemia occurs with initial manifestations of renal insufficiency.

GFR < 20-25% → the patient develops overt renal failure.

Remember that:

Azotemia → Asymptomatic

Uremia → symptomatic

Cockcroft & Gault equation: Calculation of creatinine clearance

➤ doesn't require 24hr urine collection ☺

The calculated clearance should be reduced by 15% for women.

$$\text{Creatinine clearance} = \frac{(140 - \text{Age}) \times \text{Body wt (Kg)}}{72 \times \text{Plasma Creatinine}}$$

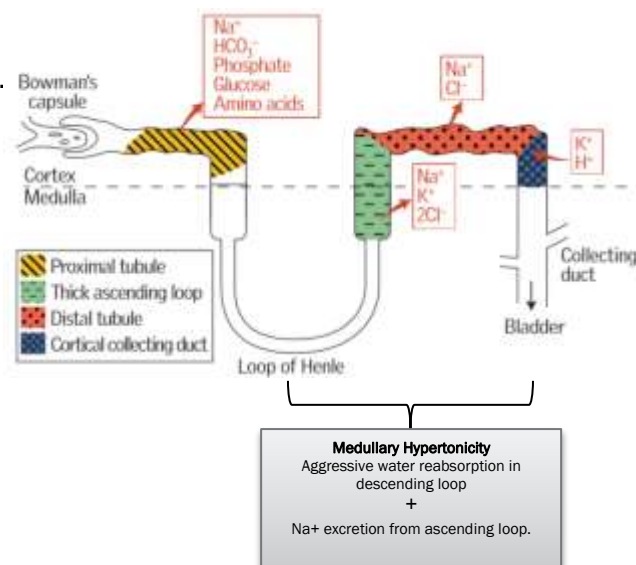
6. Cystatin-C level

It correlates better with radioisotope estimation of GFR than creatinine and more sensitive.

It is not secreted by tubules and is unaffected by gender.

Kidney function tests are classified as follows:

- **glomerular function test assessment**
 - Blood urea.
 - Serum creatinine
 - Cystatin -C Level.
 - GFR measurement by renal scan or by creatinine clearance.
- **Tubular function test assessment**
- proximal Tubular function
 - Serum K⁺ and phosphorus.
 - Glycosuria in absence of hyperglycemia
 - Amino aciduria and B2 microglobulin in urine.
- distal tubular function
 - urinary acidification by ammonium chloride test
 - Concentrating capacity by water deprivation test.



Urine analysis

Physical Examination:

1. **Color:** Normally it is amber yellow due to urochrome pigment.

- Colorless: polyuria, D.M. , DI, Compulsive H₂O intake.
- **Reddish:** Hematuria, Hemoglobinuria, Myoglobinuria. , Beetroot. Rifampicin (orange/red).
- **Brownish:** Bilirubin. Nitrofurantoin, Flagyl.
- **Bluish:** Amitriptyline.
- **Greenish:** Pseudomonas.
- **Blackish:** Alkaptonuria

2. **pH:** Normally (4.5 - 8)

Urine pH is unnecessary except in the diagnosis & treatment of RTA.

It is also helpful in the treatment of renal stones.

- Acidic urine: Normal urine, Ascorbic acid (Vit C).
- Alkaline urine:
 - o Renal tubular acidosis tubules unable to excrete H⁺).
 - o Na HCO₃ or Na citrate intake.
 - o High vegetable diet.
 - o Urinary tract infection with urea: splitting organism e.g. proteus.

3. **Specific gravity:** normally (1003-1025+)

Measurement of urine osmolality is more accurate.

- After H₂O deprivation for 12 hours it reaches 1025+.
- After plenty fluid intake it reaches 1003 or less.

Causes of Low specific gravity	Causes of High specific gravity
Diabetes insipidus	D.M
Tubulointerstitial disease	Increased proteins
Compulsive H ₂ O intake	Volume depletion

Chemical Examination:

Proteins + Glucose + proteins + ketones + Bilirubin + Urobilinogen.

Glucose: DM, pregnancy, sepsis, renal tubular damage.

Ketones: Starvation, ketoacidosis.

Nitrites: UTI, high-protein meal.

Bilirubin: Obstructive jaundice.

Urobilinogen: Pre-hepatic jaundice.

Specific gravity: Normal range: 1.000–1.030. (low SG(<1.003): diabetes insipidus, renal impairment)

pH: NR: 4.5–8

—————→ Nitrites + leukocyte esterase → Infection with G^{-ve} bacteria

Urinary proteins

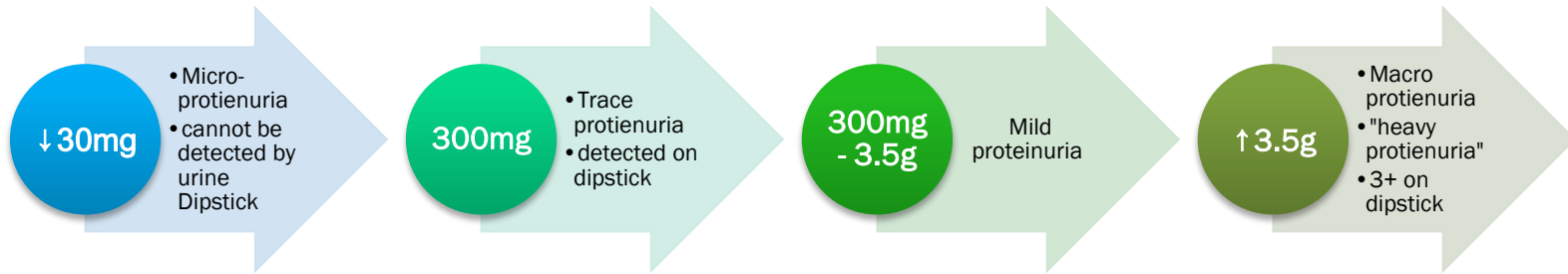
Normal urine protein = 150-200 mg/24 hr.

Normally, there is a trace of protein:

- Tamm-Horsfall protein → glycoprotein secreted by the cells of the ascending limb of the loop of Henle
- Trace of albumin.

Slightly higher values up to 300 mg daily may be excreted by adolescents.

Heavy proteinuria (↑ 3.5g /24hrs)	Mild proteinuria (↓ 3.5g / 24hrs)
Nephrotic syndrome (glomerular disease)	Nephritic syndrome
	Tubulointerstitial disease
	Orthostatic.
	Exercise
	Febrile albuminuria.
	Excessive RBCs or pus cells may give False albuminuria.
	Congestive heart failure → Congested kidney → escape of protein through the glomerulus.



Microscopic Examination of urine sediment

▪ Casts

Microscopic cylindrical structures due to coagulation of tubular protein (Tamm-Horsfall proteins) + albumin ± cellular element formed within kidney tubules.

They are formed inside the tubules → indicate upper tract lesion → nephrons.

Any excessive cells or albumin in urine causes coagulation of tubular Protein → cast formation!

The name of the cast depends on the cellular element:

- **Hyaline cast** → Nephrotic syndrome
 - Hyaline cast is seen in normal patient's urine if they're dehydrated)
 - Hyaline cast has no cellular element → Tubular protein + albumin.
- **RBC cast** → Indicates acute glomerulonephritis
- **WBC cast** → Acute pyelonephritis or Tubulointerstitial nephritis/ Transplant rejection
- **Tubular cast** → Acute tubular necrosis
- **Granular cast** → Chronic GN or chronic interstitial nephritis.

Fatty/ lipid cast → Nephrotic syndrome (common)

- Tubular protein + albumin + lipiduria.
- **Broad cast** → Cast formed in dilated kidney tubules in C.R.F
- **Waxy cast** → ESRD/chronic renal failure

URINARY CASTS

URINE MICROSCOPY

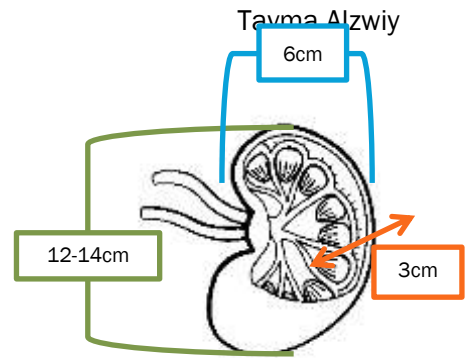


- **WCC:** >10/mm³ usually indicate UTI
- **RBCs:** >2/mm³ red cells is abnormal, indicate haematuria.
- **Casts:** cylindrical bodies formed in the lumen of distal tubules.
- **Crystals:** are common in old or cold urine and may not signify pathology. They are important in stone formers.

Ultrasound

SIZE (12x 6 x3) Cm - Bipolar length (12-14Cm)

Shrunken	Enlarged
Asymmetrical → Chronic Pyelonephritis	Hydronephrosis
	Amyloidosis
Symmetrical → Chronic G.N.	Diabetic nephropathy.
	Polycystic kidney

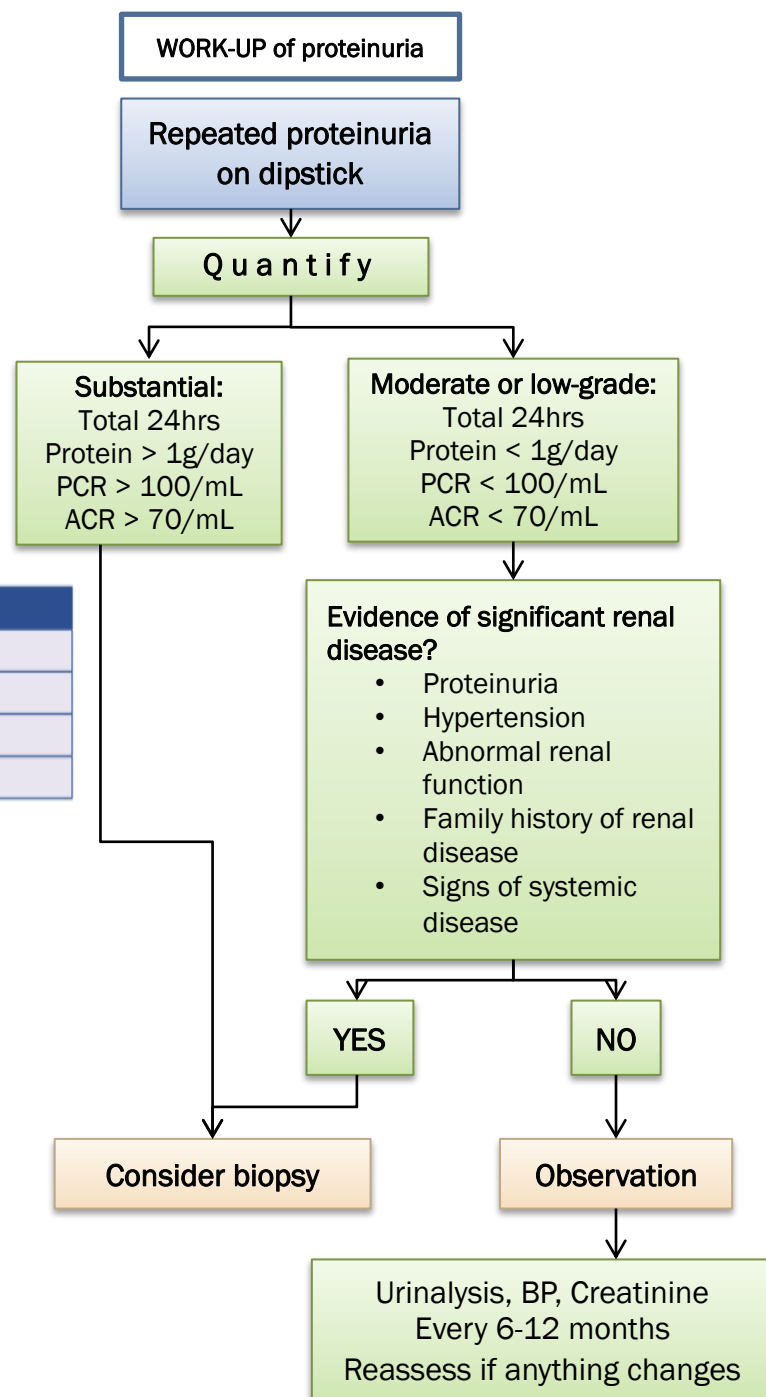
**Quick notes:**

- The first presentation of CKD due to obstruction + Hydronephrosis is medullary atrophy.
- You cannot exclude CKD because of ↑ kidney size on U/S

Proteinuria

- Normal protein excretion <150mg /24 hours (Tamm-Horsfall protein)
- Methods of assessing proteinuria:
 - 24 hr. urinary albumin excretion**
 - Normal <30mg / 24hr
 - Microalbuminuria 30-300mg/ 24hr
 - Macroalbuminuria >300mg/ 24hr
 - ACR (mg/mmol)**
 - Normal <2.5 men or 3.5 women
 - Microalbuminuria 2.5-30 men 3.5-30 women
 - Macroalbuminuria >30 in both
 - PCR**

Protein excretion g/24h	A:CR mg/mmol	P:CR mg/mmol
0.15 (physiological)	2.5 ♂ or 3.5 ♀	15
0.5	30	50
1	70	100
3 (nephrotic range)	250	300



Hematuria

Is blood in the urine → can be from anywhere in the renal tract.

- Positive dipstick confirmed by presence of RBCs on microscopy
- If positive dipstick for hematuria but negative microscopy → Hemoglobinuria OR myoglobinuria (Rhabdomyolysis).

Transient causes should be excluded, e.g. UTI, menstruation.

Classified as:

- Visible (VH): previously known as macroscopic, frank)
- Non-visible (NVH): found on dipstick/microscopy, previously known as microscopic.
 - Symptomatic (SNVH) → Lower UT Sx: Dysuria, Hesitancy, Urgency.
 - Asymptomatic (aNVH).

	Glomerular Hematuria	Non-glomerular hematuria
Type of hematuria	<u>Microscopic</u> > gross	<u>Gross</u> > microscopic
Common etiologies	- Glomerulonephritis - Basement membrane disorders (e.g. Alport syndrome)	- Nephrolithiasis - Cancer (e.g. Prostate, renal cell) - Polycystic kidney disease - Infections (e.g. Cystitis) - Papillary necrosis, renal infarction
Clinical presentation	- Nonspecific / asymptomatic - Nephritic syndrome (HTN + oliguria+ elevated creatinine)	- Dysuria or symptoms of urinary obstruction (flank pain, renal or ureteral colic, anuria)
Urinalysis	- Blood AND protein - RBC casts, dysmorphic RBCs	- Blood but NO protein - Normal appearing RBCs

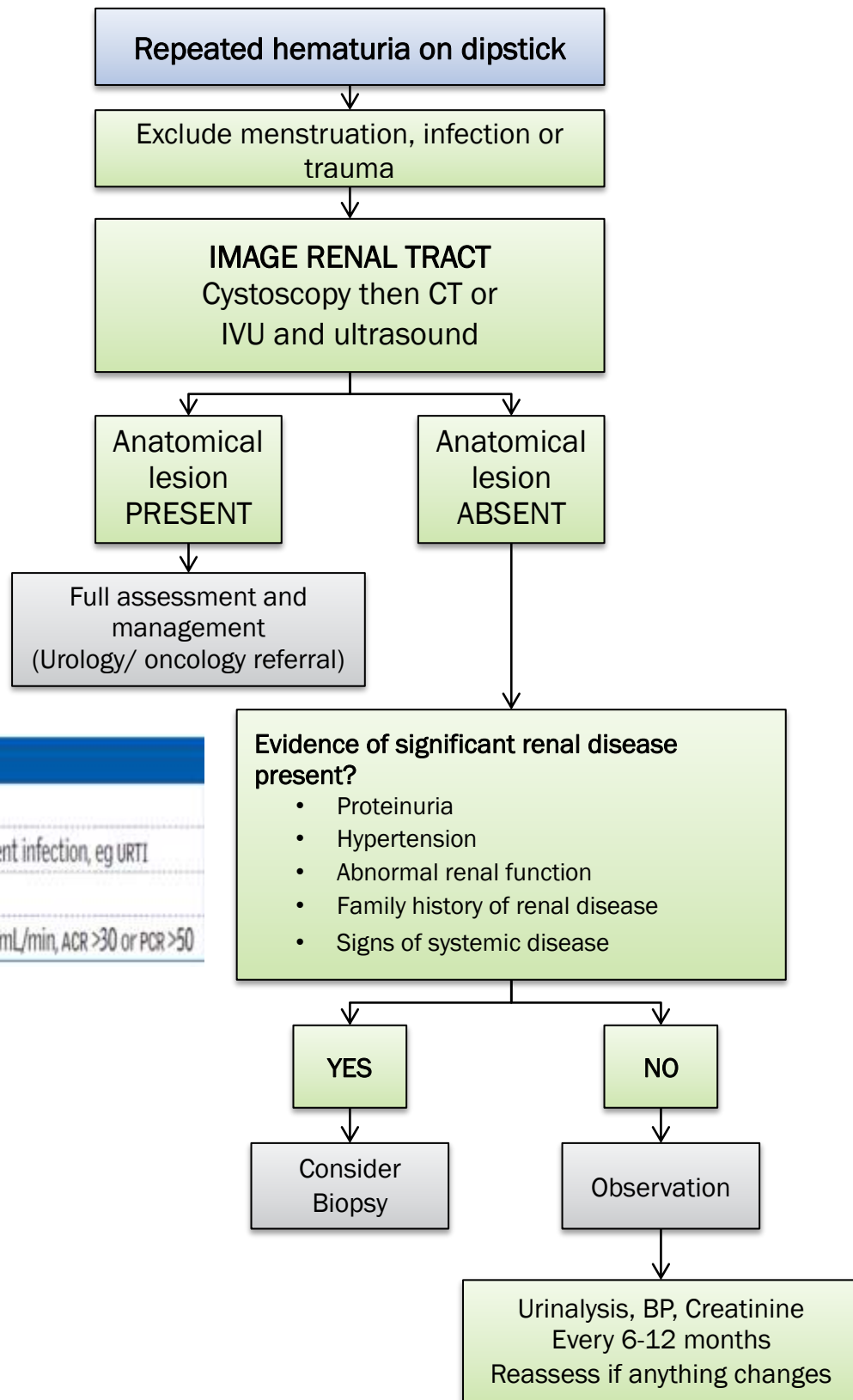
Remember that:

Nephrolithiasis → renal stones

Nephrocalcinosis → calcification of renal parenchyma

Upper collecting system	Hematuria throughout	Renal mass	Pyelonephritis
		GN	Trauma
		Urotheliasis	Urothelial cancer
		Polycystic kidney disease	
Lower collecting system	Initial hematuria	Urethritis	Trauma
	Terminal hematuria	Urotheliasis	Urothelial cancer
		Cystitis	BPH prostatic Ca.

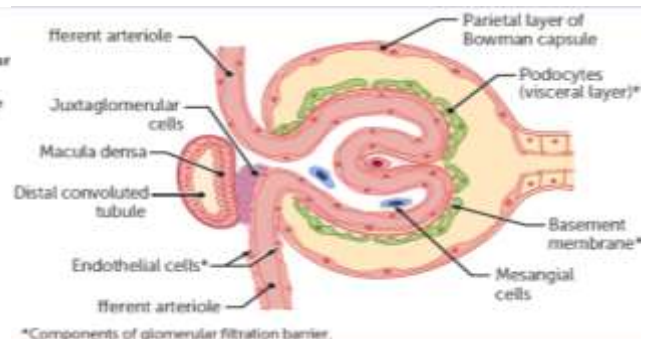
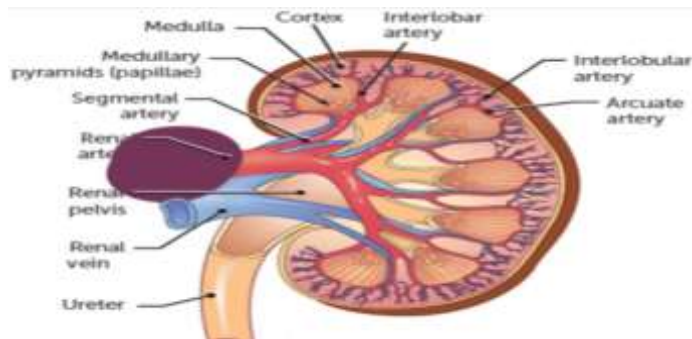
Hematuria Workup



Who to refer and to whom?

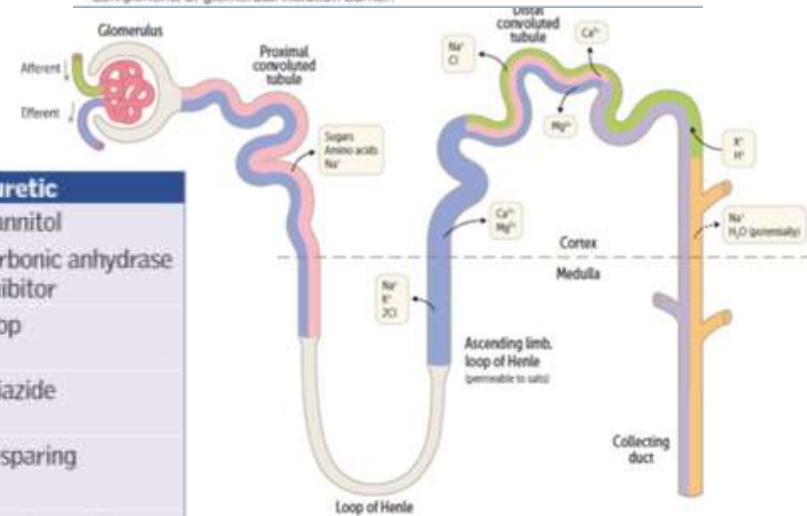
	Urology	Nephrology
VH	All patients, any age	<40yrs, cola-coloured urine, recent infection, eg URTI
sNVH	All patients, any age	
ANVH	Persistent, >40yrs	<40yrs with BP >140/90, eGFR <60mL/min, ACR >30 or PCR >50

Quick overview of Anatomy & Physiology



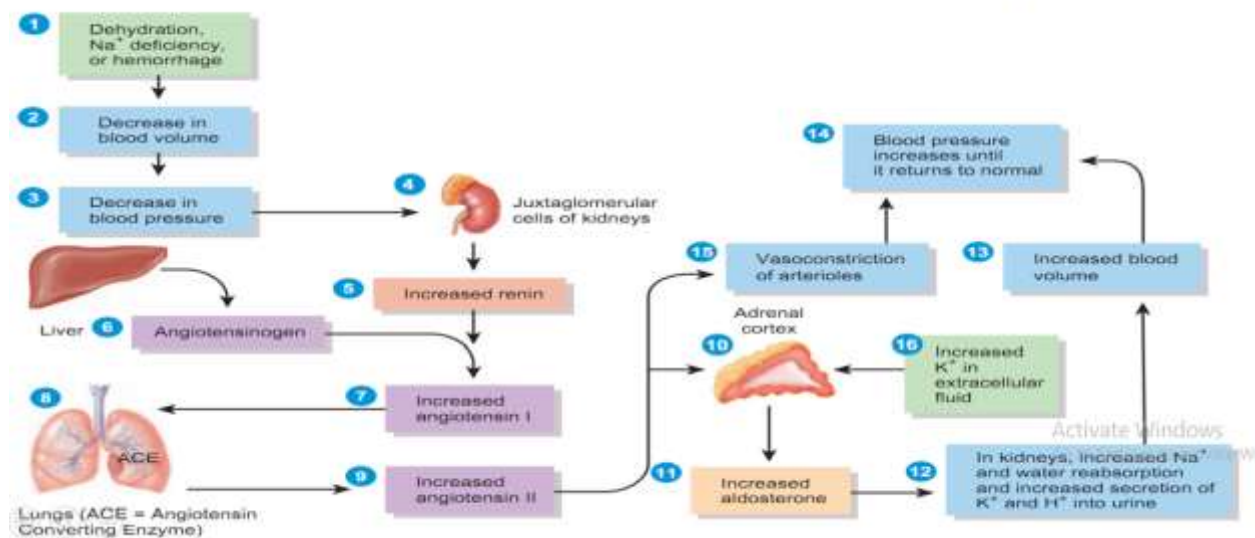
Renal Tubular function

Nephron segment	Solute movement	Tubular pathology	Diuretic
Proximal tubule	Reabsorption: Na^+ , HCO_3^- , phosphate, sugars, amino acids	Fanconi syndrome Proximal (type 2) RTA	Mannitol Carbonic anhydrase inhibitor
Thick ascending loop	Reabsorption: Na^+ , K^+ , Cl^-	Bartter syndromes	Loop
Distal tubule	Reabsorption: Na^+ , Cl^-	Gitelman syndrome	Thiazide
Cortical collecting duct	Excretion: K^+ , H^+	Distal (type 1) RTA Type 4 RTA	K^+ -sparing
Collecting duct	Excretion: water	Diabetes insipidus (p240)	v2 antagonists ('vaptan') (p320)



Renin- Angiotensin-Aldosterone-system

Aldosterone helps regulate blood volume, blood pressure, and levels of Na^+ , K^+ , and H^+ in the blood.



Acute kidney injury

Acute kidney injury (AKI) is a syndrome of decreased renal function, measured by serum creatinine or urine output, occurring over hours–days.

It includes different etiologies and may be multifactorial.

The Kidney Diseases: Improving Global Outcomes (KDIGO) guidelines 2 define AKI as:

- Rise in creatinine $>26\mu\text{mol/L}$ within 48h.
- Rise in creatinine $>1.5 \approx$ baseline (i.e. before the AKI) within 7 days.
- Urine output $<0.5\text{mL/kg/h}$ for >6 consecutive hours.

Epidemiology:

AKI is common, occurring in up to 18% of hospital patients and ~50% of ICU patients.

Risk factors:

Pre-existing CKD, age, male sex, and comorbidity (DM, cardiovascular disease, malignancy, chronic liver disease, complex surgery).

Commonest causes:

Sepsis

Major surgery

Cardiogenic shock

Other causes of hypovolaemia

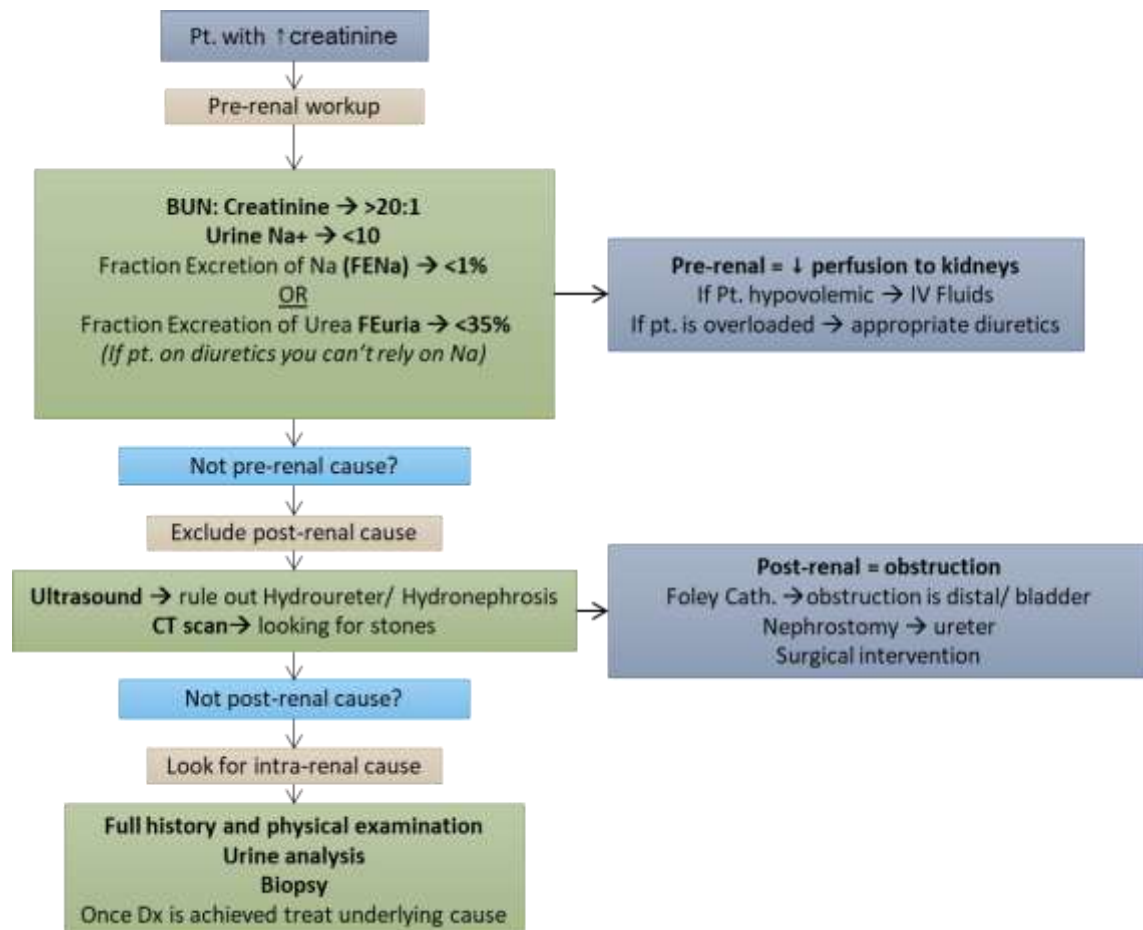
Drugs

Hepatorenal syndrome

Obstruction

Diagnostic Approach in AKI

- History (especially drug Hx) and physical examination.
- Determine the duration of renal failure $\rightarrow$ baseline Creatinine level.
- Determine whether AKI is due to prerenal, intrarenal, or postrenal causes (see next page).
- Urinalysis + chemistry (FENa^+ , osmolality, urine Na^+ , urine Cr).
- Renal ultrasound (to rule out obstruction).



Decreased blood
flow to kidney

Pre-renal

1. **Pump Failure:** MI or CHF
2. **Leaky pipes:** due to fluid in 3rd space - OSIS

PARTIALLY DUE TO

 - a. Nephrosis → nephrotic syndrome
 - b. Gastritis → protein losing enteropathies/ malnutrition
 - c. Cirrhosis
3. **Hole:** H&3D's

Decrease albumin

 - a. Diuresis
 - b. Diarrhea
 - c. Dehydration
 - d. Hemorrhage
4. **Clog:**
 - a. Fibro-muscular dysplasia: young female with HTN and Renal failure.
 - b. Renal artery stenosis: old man with atherosclerotic disease.

Intra-renal

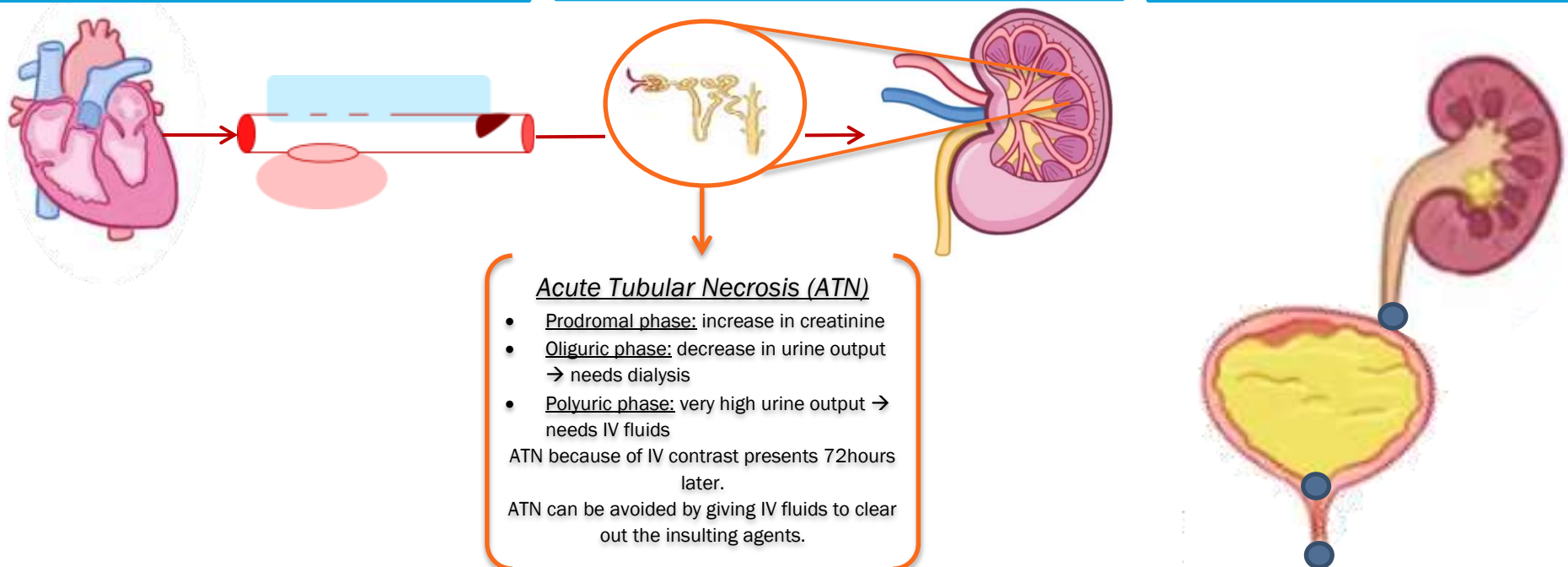
1. **Glomerulonephritis:** look for RBC cast
 - You should rule out Nephrotic syndrome → hyaline cast
 - Protein more than 3.5g/24hrs + high cholesterol + Sx of edema.
2. **Acute interstitial nephritis:** look for WBC cast + eosinophils
 - Consider pyelonephritis → infections
 - Eosinophils indicate reaction to drugs → antibiotics: TMX-SMP/ Penicillins/ cephalosporins
 - Transplant rejection..?
3. **Acute tubular necrosis:** Look for Tubular/ granular/ Muddy brown (broken down RBC's) casts.
4. Due to Ischemia → prolonged pre-renal failure 'shocked kidney'
5. Toxins:
 - IV Contrast
 - Myoglobin → Rhabdomyolysis

Post-renal

Decreased out-
flow because of
obstruction

Due to the obstruction of:

1. **Ureters:** Cancer / stone
2. **Bladder:** cancer / stone / neurogenic bladder
 - a. Drugs: α1-adrenoreceptor antagonists / antidepressants/ benzodiazepines/ hormone replacement therapies.
 - b. Spinal cord trauma!
3. **Urethra:** cancer/ stone/ benign prostatic hyperplasia/ kinked Foley catheter.



Acute Tubular Necrosis

- **Ischemic AKI → the whole tubule**
 - Secondary to severe decline in renal blood flow → shock, hemorrhage, sepsis, DIC, heart failure.
 - Ischemia results in the death of tubular cells.
- **Nephrotoxic AKI → proximal tubule affected**
 - Injury is secondary to substances that directly injury renal parenchyma and result in cell death.
 - Causes include antibiotics (aminoglycosides, vancomycin), radiocontrast agents, NSAIDs (especially in the setting of CHF), poisons, Myoglobinuria (from muscle damage, Rhabdomyolysis, Heavy exercise), Hemoglobinuria (from hemolysis), chemotherapeutic drugs (cisplatin), and kappa and gamma light chains produced in multiple myeloma.

Drugs causing nephropathy

Alteration of Renal blood flow	Acute tubular necrosis	Glomerulonephritis	Tubulointerstitial nephritis
NSAIDs ACEi/ARBs Ciclosporin	Aminoglycosides Amphotericin B NSAIDs	Gold Penicillamine	Penicillins Cephalosporins NSAIDs Allopurinol

Differentiating between Prerenal failure and ATN

	Prerenal failure	ATN
Urine osmolarity	>500	>350
Urine Na	<20	>40
FENa	< 1%	> 1%
Urine sediment	scant	Full brownish pigment + granular/ epithelial casts 'muddy brown casts'

Rhabdomyolysis

Skeletal muscle breakdown → release of intracellular contents (K⁺, myoglobin)

- ↑ Cytokines and ↓ nitric oxide cause renal vasoconstriction.
- Myoglobin is filtered by the glomeruli → obstruction and inflammation.

Presentation:

- History of: trauma, surgery, hyperthermia, **seizures**.
- Muscle pain, swelling, tenderness
- AKI / Red-brown urine.
-

Diagnosis:

- Plasma CK 5X upper limit
- ↑ K⁺ ↑ ↑ PO₄ ↓ Ca⁺
- Tea colored urine → falsely +ve for blood on dipstick
- No RBCs seen on microscopy

Treatment → supportive

- Treatment for hyperkalaemia
- IV fluid rehydration
- If oliguric, monitor CVP in ICU setting.
- Renal replacement may be needed.

Chronic kidney disease

It is a slowly progressive (within years) irreversible deterioration of kidney function with development of the clinical syndrome of uremia. The final outcome is progression to end stage renal failure.

Pathophysiology of Uremic syndrome:

Uremia refers to the syndrome resulting from the failure of the kidneys to perform their normal excretory, metabolic, and endocrine functions.

Uremia is a complex syndrome that includes a variety of physiologic and clinical abnormalities:

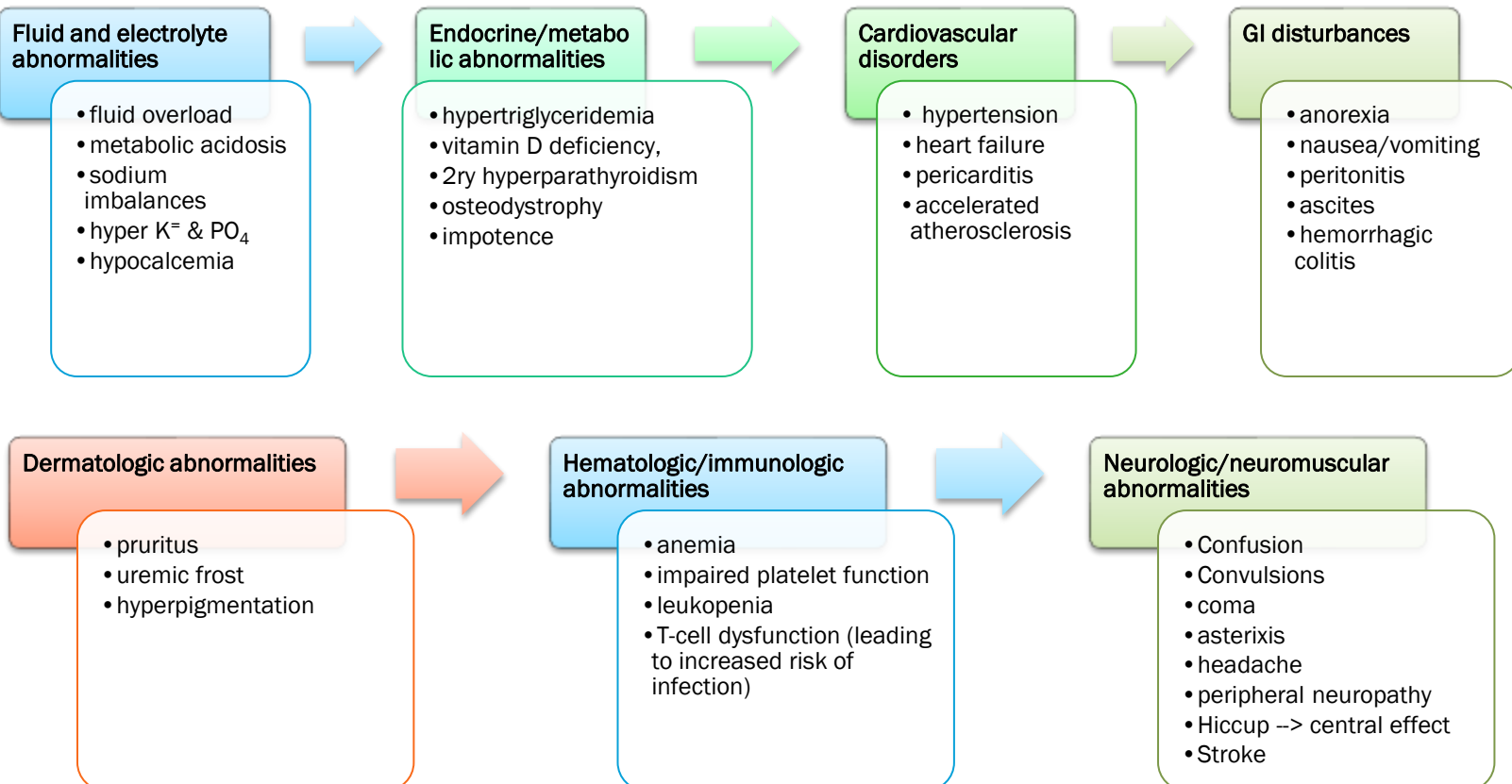
Uremic syndrome is due to the following imbalances

Increase of	Decrease of
Urea	Vit-D
Phosphate	Ca
Parathyroid hormone	Erythropoietin
Phenol	Testosterone
Guanidine	Estrogen
Indoles	
B2microglobulins	

Whenever a patient has ↑ Cr levels, the first thing to do is determine the patient's baseline Cr level, if possible.

This helps determine whether the patient has: AKI, CKD, or chronic renal insufficiency/failure with superimposed AKI. "Acute on chronic renal failure"

Leading to the following:



Causes:**COMMON**

- Diabetic nephropathy (longstanding history of D.M) → M.C.C
- Systemic hypertension (long duration).
- Chronic GN (history of puffiness).
- Undetermined etiology.
- Chronic interstitial nephritis e.g. chronic pyelonephritis (history of recurrent drug abuse).

RARE

- Obstructive uropathy, stones, bilharziasis
- Analgesic nephropathy (abuse of Paracetamol + Aspirin).
- Lupus nephritis (young + arthropathy).
- Congenital polycystic Kidney (+ve F.H).
- Gout (History of arthropathy).

Staging

Stage ^a	eGFR (ml/min/1.73 m ²)	Description	Typical testing frequency ^c
1	≥ 90	Normal or increased GFR, with other evidence of kidney damage	12 monthly
2	60–89	Slight decrease in GFR, with other evidence of kidney damage	
3A	45–59	Moderate decrease in GFR, with or without other evidence of kidney damage	6 monthly
3B	30–44		
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage	3 monthly
5	< 15	Established renal failure	6 weekly

Not having RENAL anaemia or RENAL bone disease

3B: HTN, anaemia, bone disease present

Clinical Presentation of the Complications of C.R.F

Ammoniac odor of mouth → uremic fetor (urea excreted in saliva with splitting by bacteria releasing NH₃)

Anemia

- Due to Erythropoietin deficiency.
- Decrease intake with hematinic deficiency e.g. Iron, Vit. B12, Folate.
- Bleeding tendency.
- Decreased life span of RBCs and toxic B.M depression.
- Blood loss during hemodialysis or through GIT.
- B.M fibrosis due to hyperparathyroidism
- ACE inhibitors may decrease erythropoietin release → anemia (Rare side effect).

DDx CKD without/ with mild anemia

1. Early stages
2. High erythropoietin:
 - Poly Cystic Kidney Disease
 - Hypernephroma
 - Hydronephrosis

Bleeding tendency

- Capillary fragility.
- Thromboasthenia due to the uremic toxins.

CVS

- Pericarditis (indication for dialysis).
 - Uremic toxins irritate the pericardium.
 - Feature of severe pre-terminal uremia or inadequate dialysis.
 - It usually resolves with intensive dialysis.

- Hemorrhagic pericardial effusion with the danger of pericardial tamponade may occur.
 - Anticoagulants should be used with caution.
- Systolic and diastolic dysfunctions are also common.
 - Diastolic dysfunction is due to LVH & contributes to hypotension during fluid removal and hemodialysis.
 - Systolic dysfunction is due to myocardial fibrosis, abnormal myocyte function, myocardial calcification.
- Arrhythmias → electrolyte disturbances.
- Hypertension → salt and H₂O retention and hyper-reninism
 - CKD with normal BP or hypotension
 - Salt losing nephropathy ——— Tubulointerstitial diseases.
 - Hypo-reninism — Diabetic, interstitial, obstructive nephropathy.

DM

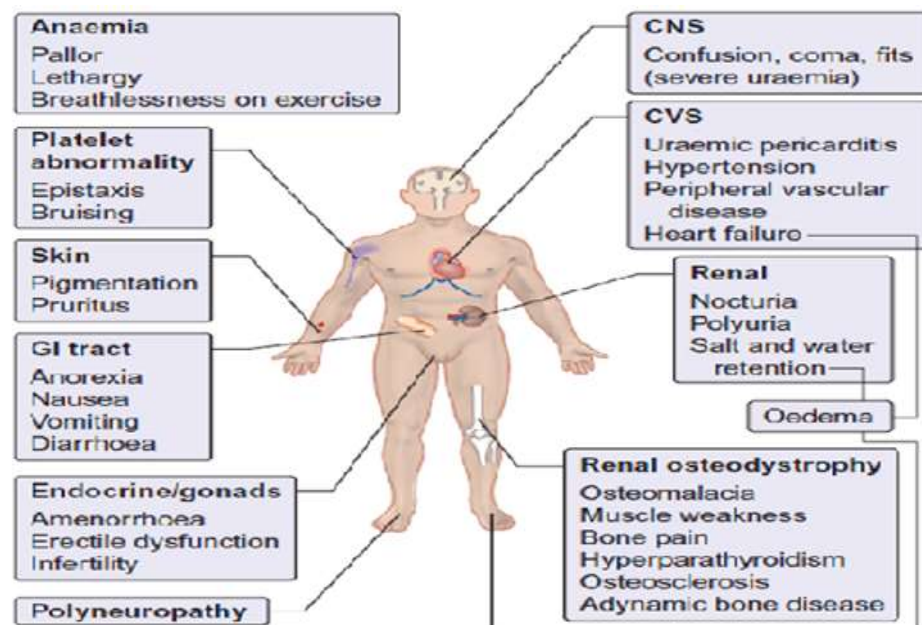
- Insulin Resistance: Impaired glucose tolerance and not D.M (uremic pseudo diabetes).
- Insulin excreted by the kidney so insulin requirements in diabetic patient with renal impairment will be decreased.

Thyroid dysfunction

Sluggish TSH release → elevates TRH → release of prolactin + decrease prolactin clearance → Amenorrhea, galactorrhea & Impotence.

Endocrine & metabolism

- Low Ca → 2ry hyperparathyroidism.
- Impaired clearance of TAG & hypercholesterolemia may occur.
- Decreased serum testosterone level with impotence and decreases spermatogenesis.



Acid base & electrolytes

K⁺, PO₄³⁻, AL³⁺, H⁺ (excreted through the kidney).

- Hyperkalemia
- Hyperphosphatemia
- Metabolic acidosis (↓ pH).
- High aluminum levels.
- Low Ca levels → normal → high.
- **Na and water retention with normal sodium level.**
Hyponatremia may occur due to excessive ingestion of water
Hypernatremia is infrequent in chronic renal failure.

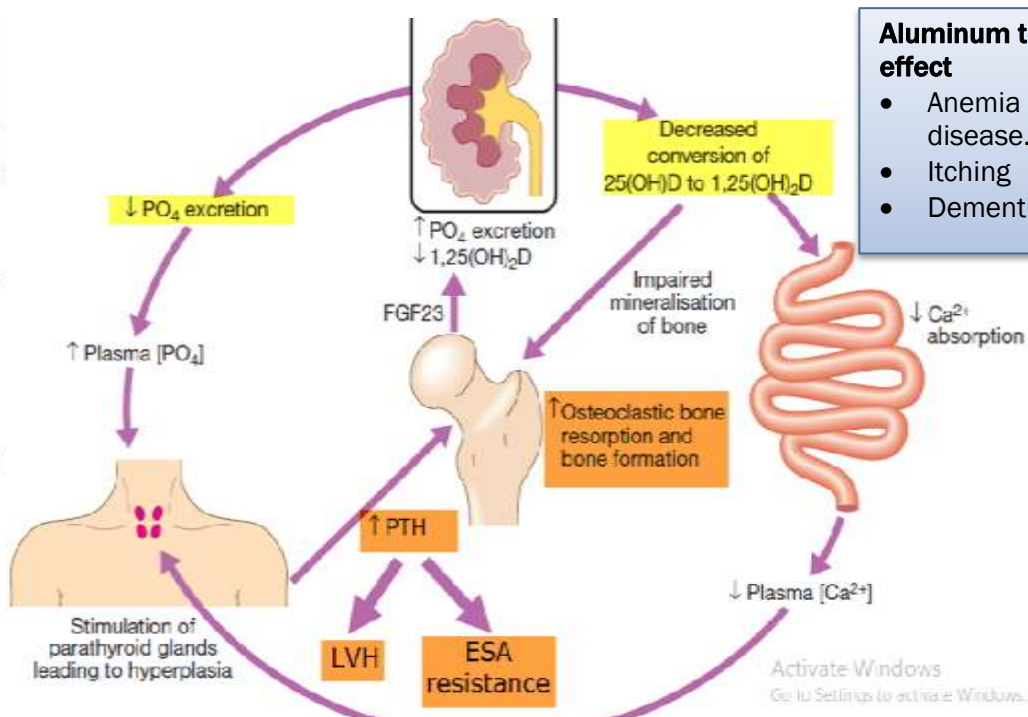
Bone disease (renal osteodystrophy)

Impaired mineralization also occurs with aluminum toxicity due to phosphorus binders containing aluminum or exposure to aluminum in water source used to make up dialysate fluids for hemodialysis.

RENAL BONE DISEASE

Components of CKD-MBD:

1. High PO_4
2. Low Ca
3. 2ry hyperparathyroidism
4. Low Vitamin D level
5. Acidosis: increase severity of bone disease
6. Ectopic calcification (high PO_4 combine with Ca in blood vessels and other tissues)



Chest

Pneumonia (because of ↓ immunity) + Non cardiogenic pulmonary edema + Acidotic breathing

Neurological

- **Neuropathy**
 - Motor Weakness.
 - Sensory Glove & Stock hypoesthesia.
 - Autonomic neuropathy → Impotence/ Diarrhea & Constipation.
 - Carpal tunnel syndrome due to amyloidosis (B2 microglobulin deposition)
- **Restless legs syndrome**

(Irresistible need to move legs, often interfering with sleep)

Disequilibrium syndrome → due to rapid decrease of blood urea by intensive dialysis (Brain edema).

Dialysis Dementia → (Aluminum related), or microcytic anemia.

Skin

Itching due to:

Hyperparathyroidism + Hyperphosphatemia + Hypercalcemia (due to Ca^{+} containing Phosphate binders + vit D).

Prognosis

GFR and albuminuria are independently associated with a higher risk of:

- All-cause mortality
- Cardiovascular mortality
- Progressive kidney disease and kidney failure
- AKI.

Remember that giving Ca⁺ Channel blockers + ACE Inhibitors will reverse the progression of proteinuria!

Risk factors increase the progression of CKD

- Vascular volume depletion: Diuretic, GIT loss, low COP, Nephrotic syndrome, liver disease with ascites.
- Nephrotoxic agents:- NSAID , Aminoglycosides , vancomycin , contrast
- UT obstruction: BPH, stone.
- Infection: sepsis, UTI.
- Metabolic: DM, Obesity, hyperlipidemia, hypercalcemia, hyperphosphatemia.
- High protein diet.
- Smoking.

KEY POINTS

- CKD most often occurs as a complication of a chronic systemic illness. In the United States, the leading conditions are diabetes and hypertension.
- Early detection and treatment of CKD can delay or prevent the progression to more advanced stages and to end-stage renal disease.
- Monitoring of CKD involves serial calculation of estimated GFR (based on the plasma creatinine) and monitoring for the development of proteinuria.
- Progressive CKD can lead to the syndrome of uremia, which is manifested as signs and symptoms related to the loss of the excretory, metabolic, and endocrine functions normally performed by the kidneys.
- When conservative treatment (fluid and electrolyte management, dietary modification) fails, patients require more aggressive treatment and advanced planning for dialysis may be indicated

Investigation

To prove renal failure:

1. Blood Urea → HIGH
2. serum creatinine → HIGH
3. K → HIGH
4. PH → LOW

To prove chronicity

1. Low Ca & Hb
2. High phosphate.
3. Broad casts in urine.
4. Low fixed specific gravity (1010) = Isosthenuria.

May also be present in acute kidney injury

To prove chronicity

U/S (most important)

Shrunken kidney.
Advanced Hydronephrosis
Polycystic kidney.
Poor differentiation between cortex & medulla (parenchymal disease).

DDx CDK with normal/large kidney:

- Diabetes
- Amyloidosis
- Multiple Myeloma
- Adult polycystic kidney disease

Looking for causes to control any reversible factors if possible:Urine analysis for:

- Pus cells → active bacterial infection
- RBC casts → glomerulonephritis.
- Plain X-ray → stones.
- U/S → stones or Hydronephrosis.
- Markers for S.L.E.
- Eosinophilia → vasculitis or allergic Tubulointerstitial nephritis.

Management Goals

1. Identify and treat reversible causes:
 - a. Stop all nephrotoxic drugs
 - b. Treat UTI, stones, obstructions if present
 - c. Treat any systemic diseases + **ADJUST THE DOSE OF SUB Q MEDICATION ACCORDING TO GFR** (Heparin + Insulin)
2. Prevent the progression of CKD

Control BP "most important" :
 Target: <130/80
 Best anti-HTN: ACE-i and ARBs
 N.B. CKD + No diabetes + ACR <30 + HTN ►
 follow NICE guidelines of HTN

ACE-i and ARBs : indications in CKD (NICE)

1. In Diabetes:
 - a. HTN
 - b. ACR > 2.5 (men), 3.5 (women) with or without HTN
2. No Diabetes:
 - a. HTN + ACR ≥ 30 mg/mmol
 - b. ACR ≥ 70 mg/mmol with or without HTN

Tight Glycemic Control
 Stop smoking
 Statins for Hypercholesterolemia
 Normal protein diet

3. Treat the complications and symptoms
4. Renal replacement therapy in end stage patients

Step 1: conservative (medical) treatment

1. Maintain a good general health condition by minimizing symptoms → Stable CKD
2. Serum Creatinine <8 mg/dl (if patient is Diabetic <6 mg/dl)
3. Blood urea < 200 mg/dl.

The above 3 indications must be fulfilled together.

Note: statins have no role in patients on dialysis.

Step 2: Diet control**1. Protein:**

A Low protein diet decreases GFR so reduces progression of glomerulosclerosis.
 Also protein restriction reduces phosphate load → think renal bone disease.

Prolonged Protein restriction should be avoided to avoid low immunity
No protein restriction on patients on dialysis.

2. **Carbohydrate** (source of energy 250 gm. /d).
3. **Low potassium diet** (fruits & citrus fruits).
4. **Sodium:** If there is salt retention (in most patients), restrict Na.
In cases of salt losing nephropathy → Tubulointerstitial disease → give Na supplements.
5. **Fluid intake:** (the fluid intake = 500 cc + volume of urine in the previous day).
To avoid Dilutional hyponatremia.

Step 3: Symptomatic therapy

- **GIT**
 - Domperidone → Vomiting & Hiccough.
 - PPI → Gastritis.
- **Endocrinal disturbances**
 - Ca supplements ——— Calcium carbonate oral.
 - Vitamin D (one alpha) ———It is a synthetic analogue of vit D (1- α -calcidiol).
 - Hyperprolactinemia is treated by bromocriptine.
- **Management of CKD Bone Metabolic disorders:**
 1. Phosphate binders:
 - a. Non-calcium containing → the best → SEVELAMER
 - b. Calcium containing → Ca Carbonate, Calcium Acetate
 2. Vitamin D → Active form (Calcitriol, 1- α Calcidiol)
 3. Correct acidosis → decrease the use of bone Ca as a buffering agent!
 4. Cinacalcet or Parathyroidectomy in pt. is 3rd Hyperparathyroidism
- **Anemia:**

Target hemoglobin of 10-12 gm. /dl.

- Iron therapy is helpful especially iron infusion (mucosal edema means that the pt. can't absorb well, avoid giving oral treatment and stick to parenteral route).
- Erythropoietin (ESA) → The starting dose is 50 u/Kg/ 3x a week.
 - o Is a synthetic product and thus has multiple side effects:

Side-effects of erythropoietin

- accelerated hypertension potentially leading to encephalopathy and seizures (blood pressure increases in 25% of patients)
- bone aches
- flu-like symptoms
- skin rashes, urticaria
- pure red cell aplasia* (due to antibodies against erythropoietin)
- raised PCV increases risk of thrombosis (e.g. Fistula)
- iron deficiency 2nd to increased erythropoiesis

Treatment target:

Serum PO₄: <1.7 mmol/L / <5.3 mg/dL

Serum Ca²⁺: 2.2 -2.45

PTH: <3x Upper limit of normal
(<200pg/ml)

NOTE: Polycythemia due to kidney

1. Hypernephrosis
2. Hydronephrosis
3. Polycystic kidney

- Avoidance of blood transfusion because of increased chance of infection and sensitization to HLA antigens, which increases the risk of rejection of transplanted kidney in the future.
- Failure to respond to adequate dose of erythropoietin may be due to iron deficiency, bleeding, malignancy, infection, Aluminum toxicity, BM failure.
- **CVS manifestations:**
 - Hypertension → ACE/ Ca Channel blockers, Diuretics → ACE inhibitors combined with CCBs have proven to control BP and reverse the progression of Microalbuminuria.
 - Pericarditis: It is an indication of dialysis.
 - Heart failure & Arrhythmia: Combination of antihypertension agent is useful (Diuretics) to correct sodium and water retention.
 - Lipid lowering agents unless patient is on dialysis.
- **Impotence:** Can be treated by Sildenafil.
- **Acid base & electrolyte disturbance:**
 - Dietary restriction of potassium intake.
 - Cation exchange resins to remove potassium in GIT. Polystyrene sulphonate resins with a Laxative, kayexalate.
 - Glucose insulin infusion → if there is no response → dialysis.
 - **Acidosis correction**
 - is helps to correct hyperkalemia
 - Sodium bicarbonate, but it may cause fluid retention.
 - Calcium carbonate used as calcium supplement and phosphate binder as it plays a role in the buffering system → If there no response → dialysis.
- **Pruritus:** is improved by controlling $\text{Ca}^+ / \text{PO}_4$ balance and hyperparathyroidism.
 - Antihistamines, oral charcoal and ultraviolet photo therapy are helpful.

Step 4: Lastly treat any reversible factors

- Remove stones
- Treat UTI
- D.M → control to the lowest HbA1C possible without any hypoglycemic episodes.
- Hypertension → control.
- Avoid nephrotoxic drugs.
- Follow up monthly with periodic investigations for creatinine, Urea, Na^+ , K^+ , Hb, Ca^+ and PO_4 .

Indications for dialysis in CKD

- Bad general condition.
- S. Cr. > 8 mg/dL and > 6 mg/dL in D.M or GFR < 10 ml/min for non-diabetics and GFR < 15ml/min for diabetics.
- Blood urea > 200 mg/dL.

One indication is enough to start dialysis.

POTASSIUM DISTURBANCES – HYPERKALEMIA

A plasma potassium $>6.5\text{mmol/L}$ is a potential emergency and needs urgent assessment. The worry is of myocardial hyper-excitability leading to ventricular fibrillation and cardiac arrest. First assess the patient—do they look unwell, is there an obvious cause? If not, could it be an artefactual result?

Concerning signs and symptoms

Fast irregular pulse
Chest pain
Weakness
Palpitations
Light-headedness

ECG:

1st Tall tented T waves

2nd Wide QRS complex

3rd Small P waves

→ Ventricular fibrillation → Asystole

Artefactual results “pseudo $\uparrow K$ ”: If the patient has no SxS or ECG changes:

- Hemolysis: Difficult vene-puncture (patient clenched fist/ tight tourniquet) excessive tube shaking...
- Contamination with potassium EDTA anticoagulant in CBC bottles.
- Thrombocythaemia (K^+ leaks out of platelets during clotting)
- Delayed analysis (K^+ leaks out of RBCs; a particular problem in a primary care setting due to long transit times to the lab).

Causes

- Oliguric renal failure → AKI/CKD
- K^+ -sparing diuretics.
- Metabolic acidosis (DM)
- Excess K^+ therapy.
- Addison's disease
- Massive blood transfusion.

Academia and hyperkalemia occur together when the body tries to buffer the blood

- Burns.
- Drugs, e.g. ACE-i, suxamethonium.
- Artefactual results 'Pseudo hyperkalemia'
- Any α -lysis in the body → K^+ shift (tumor lysis Sx, Rhabdomyolysis)

Management:

Listen: if you see a big K^+ the patient is going to die...

C

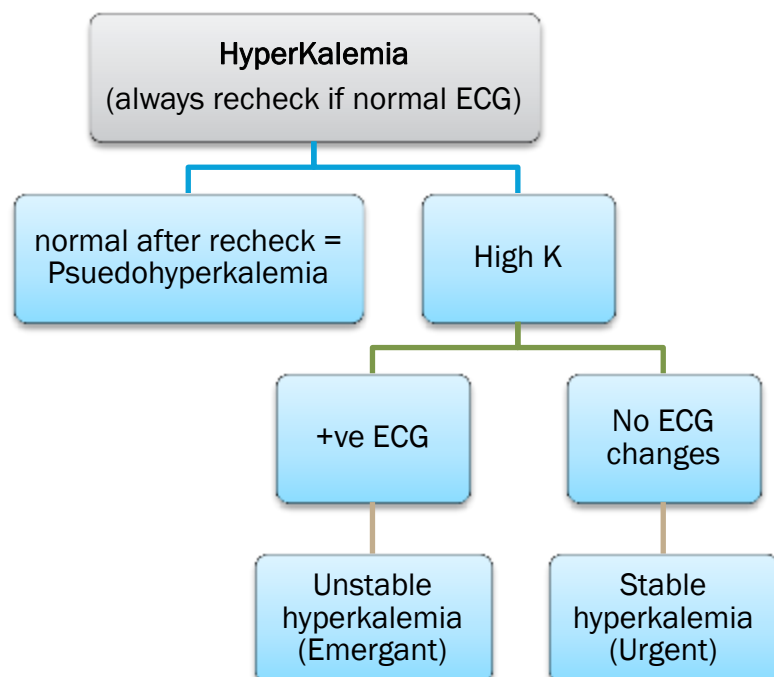
BIG

K

DI

C BIG K DI (calcium, bicarbonate/beta-agonist, insulin, glucose, Kayexalate, Diuretics/ Dialysis).

1. Stabilize calcium gluconate (IV). protect heart always first step
2. Temporize (shift potassium inside cells). Takes Hours for correction
 - insulin + D50
 - Na HCO₃
 - B-agonist
3. Decrease total body potassium , TAKES DAYS
 - Stool (kayexalate).
 - Urine (diuretics).
4. Dialysis if on dialysis already OR Acute dialysis if not responding.



POTASSIUM DISTURBANCES – HYPOKALEMIA

If $K^+ < 2.5 \text{ mmol/L}$, urgent treatment is required.

Note: Hypokalemia exacerbates digoxin toxicity.

Signs and symptoms

- Muscle weakness
- Hypotonia
- hyporeflexia
- cramps
- tetany
- palpitations
- light-headedness (arrhythmias)
- constipation.

ECG

- Small or inverted T waves
- prominent U waves (after T wave)
- Long PR interval
- depressed ST segments

Causes

- Diuretics
- Vomiting and diarrhoea.
- Pyloric stenosis.
- Cushing's syndrome/steroids/ACTH.
- Conn's syndrome → suspect if the pt. is Hypertensive.
- Alkalosis
- Renal tubular failure

If Mg is low → hypokalemia is difficult to correct until Mg levels are normalized.

Management

If Mild → $> 2.5 \text{ mmol/L}$ + no symptoms

- Give oral K^+ supplement and/ or potassium sparing diuretics.
- Review K^+ after 3 days.

If severe: → $< 2.5 \text{ mmol/L}$, and/or dangerous symptoms.

- Give IV potassium chloride slow infusion in IV drip CAUSIOUSLY.

Do not give K^+ if oliguric.

Never give K^+ as a fast STAT bolus dose.

Tumor lysis syndrome

Occurs mainly during the induction phase of chemotherapy for rapidly proliferating tumors (leukemia, lymphoma, and myeloma).

Leads to cell death → $\uparrow$ Urate, $\uparrow$ K^+ , $\uparrow$ phosphate, $\downarrow$ calcium.

- Risk of arrhythmia and renal failure.

Management: Prevent with hydration and uricolytics, e.g. rasburicase (BEST), allopurinol.

Monitor K^+

Renal Replacement therapy – RRT

Dialysis and Filtration

Indications for dialysis: **AEIOU**

A → Acidosis

E → Electrolytes (Na/K)

I → Ingestion of TOXINS

O → Overload (CHF, Edema)

U → Uremia (pericarditis, encephalitis .etc)

- inability to control volume status, including pulmonary oedema
- inability to control blood pressure
- serositis
- acid-base or electrolyte abnormalities
- pruritus
- nausea/vomiting/deterioration in nutritional status
- cognitive impairment.

Disequilibrium syndrome

Rapid correction of all of the following causes brain edema → Confusion, Convulsion, Coma → DEATH

Na⁺

Glucose

Urea

Complications of RRT Annual mortality is significant, mostly due to

Cardiovascular disease: BP, calcium/phosphate dysregulation, vascular stiff ness, inflammation, oxidative stress, abnormal endothelial function.

- **Protein-calorie malnutrition:** Increases morbidity and mortality.
- **Renal bone disease:** High bone turnover, renal osteodystrophy, osteitis fibrosa.
- **Infection:** Uraemia causes granulocyte and T-cell dysfunction with ↑ sepsis-related mortality.
- **Amyloid:** B2-microglobulin accumulates in long-term dialysis causing carpal tunnel syndrome, arthralgia, and visceral effects.

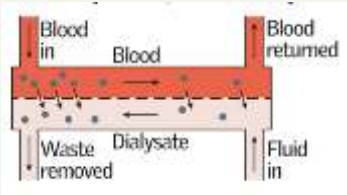
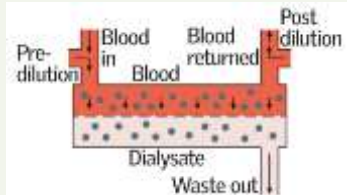
Indications of Nephrectomy prior to renal transplantation:

1. Pyonephrosis
2. Massive PKD
3. Uncontrolled HTN
4. Renal/ Urothelial Malignancy

Fistula

- For fistula to reach full arterialization it requires 60 days → you can start using it after 30 days if necessary
- How to know if the fistula is functional:
 1. Thrill felt
 2. Bruit on auscultation
 3. Recent instrumentation markings

Duplex is GOLD standard

	Hemodialysis	Peritoneal dialysis	Hemofiltration
Access	AV fistula Tunneled venous access	Tenckhoff catheter	AV fistula
Principle	Blood is passed over a semi-permeable membrane against dialysis fluid flowing in the opposite direction. Diffusion of solutes occurs down the concentration gradient. A hydrostatic gradient is used to clear excess fluid as required (ultrafiltration). 	Uses the peritoneum as a semi-permeable membrane. A catheter is inserted into the peritoneal cavity and fluid infused. Solutes diffuse slowly across. Ultrafiltration is achieved by adding osmotic agents (glucose, glucose polymers) to the fluid.	Water cleared by positive pressure, dragging solutes into the waste by convection. The ultrafiltrate (waste) is replaced with an appropriate volume of ('clean') fluid either before (predilution) or after (post-dilution) the membrane. 
Problems	• Access – arteriovenous fistula: thrombosis, stenosis, steal syndrome; – tunneled venous line: infection, blockage, recirculation of blood), • Disequilibrium syndrome: (between cerebral and blood solutes leading to cerebral edema • Hypotension • Time consuming.	• Catheter site infection • Peritonitis • Hernia • Loss of membrane functions over time.	• Time consuming.
Extra notes		Is contraindicated in patients who have 1. chronic severe chest disease 2. active intraabdominal infections 3. pt who are physically / mentally incapable.	

Renal Transplant

Renal transplant is the treatment of choice of end stage kidney disease ESKD.

Types of grafts

- Living donor: Best graft function and survival, especially if HLA matched.
- Deceased donor:
 - Donor after brain death (DBD, (heart-beating donor).
 - Expanded criteria donor (ECD) is from an older kidney or from a patient with a history of CVA, BP, or CKD. This impacts on the long-term prognosis of the transplant but offers a better outcome than remaining on dialysis.
 - Donor after cardiac death (DCD, non-heart-beating donor) with increased risk of delayed graft function.

Matching for renal transplant:

1. Blood group compatibility → Most important!
2. HLA- Matching → (DRawBACK)
 - DR > B > A > C

Contraindications

- Absolute: cancer with metastases.
- Temporary: active infection, HIV with viral replication, unstable CVD.
- Relative: congestive heart failure, CVD.

Post-operative problems

1. Acute tubular necrosis of graft
2. Vascular thrombosis
3. Urine leakage
4. UTI

Recurrence of renal pathologies post-renal transplantation:

1. Membranoproliferative GN: 40-90%
2. FSGS: 40%.
3. Membranous GN: 30%.
4. IgA

Complications

- Surgical: Bleed, thrombosis, infection, urinary leaks, lymphocele, hernia.
- Delayed graft function: Affects up to 40% of grafts, more common in DCD.
- Rejection:
- Infection: 1. CMV is the most common (+1 mth)
- 2. Pneumocystis jirovecii → excruciating Dyspnea
- 3. Reactivation of TB
- Malignancy → Sq. cell Ca (Skin cancer is most common) / NH Lymphoma
- CVS → MCC of death in transplant patients (HTN/ Drug side effects)
- Osteoporosis → long term steroid use
- Drug S/E

Type of rejection	Hyperacute	Acute	chronic
Frequency	<1%	50%	50%
Onset after transplant	<48 hrs	<6 months	>6 months

Bacterial infections occur ↓ 1 month

Acute graft rejection may be:

1. Antibody mediated
2. Cellular rejection → M.C
3. Vascular

Immunosuppression in Renal transplant patients

1. Induction → Monoclonal antibodies (basiliximab, (selectively block activated T cells) BEST / Alemtuzumab (T- and B-cell depletion).
2. Maintenance:
 - Calcineurin inhibitors → Tacrolimus or ciclosporin → *Diarrhea, nephrotoxic, HTN.*
 - Antimetabolites → Mycophenolic acid (MPA), azathioprine → *Anemia, leucopenia, liver enz derangement, MPA is teratogenic, can't give Allopurinol w/ Azathioprine*
 - Prednisolone

Glomerular disease

General points

- they are generally chronic
- they are generally not caused by hypoperfusion or toxins
- ALL OF THEM CAUSE NEPHROTIC SYNDROME
- Biopsy is the most accurate test to establish a diagnosis → But not always needed...
- Often treated with steroids and resolve spontaneously
 - Additional medications in form of Immunosuppressives (cyclophosphamides) are also frequently used.
- Primary GN has no systemic involvement → local manifestations only
- Secondary GN 3Is and 3Ms (causes both Nephritic and Nephrotic)
 - Infections → streptococcus (M.C)
 - Immunological → SLE (M.C)
 - Iatrogenic → Rheumatology Rx (M.C)
 - Metabolic → D.M / Amyloidosis
 - Malignancy → Multiple Myeloma / Lymphoma
 - Miscellaneous causes

Immunological presentation because of:

1. Deposition of: Ab + Ag complex & complement
2. Antibody mediated
3. Abnormal complement activation

Diagnostics

All forms of glomerulonephritis have:

- Urinalysis w/ hematuria
- Dysmorphic RBCs
- Red cell casts
- Urine sodium and FENa are **LOW**
- Proteinuria → To some degree

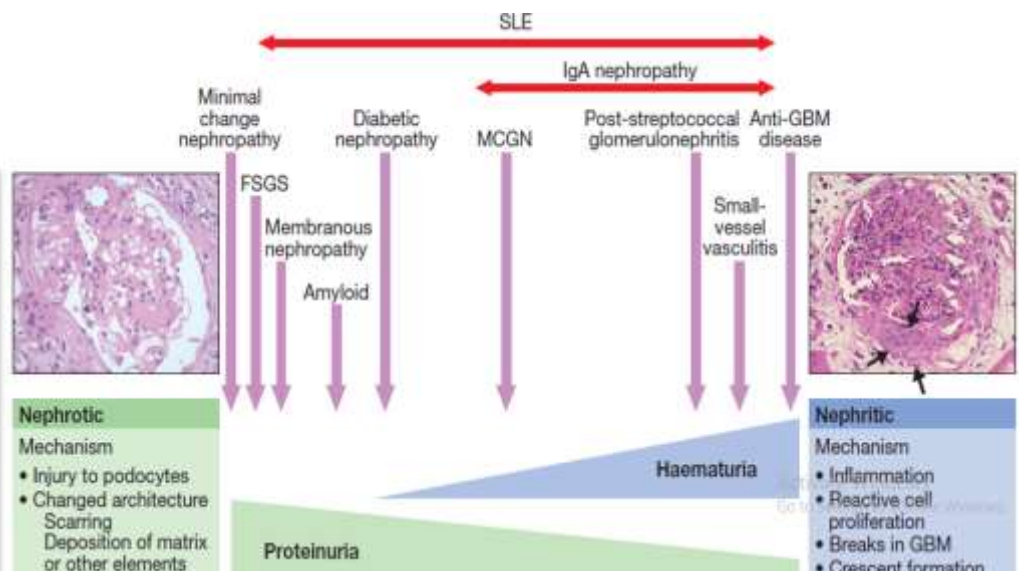
Presentation of GN

- Nephrotic
- Nephritic
- Proteinuria
- Hematuria
- AKI
- ESKD

It may just present with hypertension!

→ Glomerulonephritis with ↓ complement

- Postinfectious GN (e.g., endocarditis, Group A streptococcal infection)
- SLE
- Cryoglobulinemia
- Membranoproliferative GN
- Atheroembolic disease



Disease	Minimal change GN	Membranous GN	Membrano-proliferative GN	Focal Segmental GN
	← All present with NEPHROTIC →			
Key points	- NSAIDS + Hodgkins Lymphoma - Normal creatinine & Light microscopy - Disease of pediatric age group → MCC of GN in kids.	- Idiopathic - M.C.C of GN in Adults - Hepatitis B - SLE - Renal vein thrombosis - Antiphospholipase A2 Ab	- Hepatitis C (+70%) - Bacterial endocarditis - Malaria - Hodgkins Lymphoma / CLL	- Adults and children - M.C.C is IDIOPATHIC - Black males - HIV +ve - Heroin
Prognosis	Good	Not so good 1/3 of patients progress to CKD → ESKD	POOR 50% → ESKD May recur even posttransplant	25% progress to ESKD
Diagnosis	Bx(if 3x episodes of edema) → electron microscopy: Fusion of podocytes.	Bx → Granular IgG	Bx → Electron dense deposits	Bx → sclerosis & hyaline deposits
Treatment	General Rx Statins for high lipid profile + Anticoagulation for thrombotic complications + low salt intake and loop diuretics for edema			← and ACEi/ARBs to Rx the HTN

Disease	IgA nephropathy	Post-streptococcal GN	Good pasture Syndrome Anti-GBM
Key points	- M.C.C of Acute GN in young adults. - More in males - MACROSCOPIC Hematuria within 3 days post URTI	- ACUTE nephritic syndrome - Proteinuria & LOW COMPLEMENT - MACROSCOPIC Hematuria within 1-2 weeks days post URTI	- Bleeding in Lungs and kidneys - smoker - No other signs of systemic vasculitis
Prognosis	Good → macroscopic hematuria Bad → males, HTN, Proteinuria [RECURS POST TRANSPLANT]	Very good Spontaneous recovery	Poor if pt. is dialysis dependent on presentation
Diagnosis	Bx → IgA deposits + mesangial proliferation	Increased Anti-Streptolysin O Bx → Granular IgG 'HUMPS' C3 deposition Diffused proliferation	Anti-GBM antibodies Crescentic proliferation Bx → lung/ kidney → Linear deposits IgG
Treatment	BP control with ACEi/ARBs Steroids indicated if - Proteinuria >1g & declining GFR - Nephrotic syndrome	Supportive Rx Antibiotics + Diuretics if overloaded	Plasmapheresis and steroids +/- Cyclophosphamide

Rapidly progressive GN + vasculitis

Rapidly progressive GN

Any aggressive GN, rapidly progressing to renal failure over days or weeks and ending by end stage kidney disease.

Causes:

- Small vessel/ANCA vasculitis
- Lupus nephritis
- Anti-GBM disease
- Other GNs may 'transform' to become rapidly progressive including IgA and membranous GN.

Diagnosis:

Breaks in the GBM allow an influx of inflammatory cells so that **crenscents** are seen on renal biopsy (may be referred to as crescentic GN)

Treatment:

- Corticosteroids and cyclophosphamide.
- Other treatments depend on the etiology
- Plasma exchange → anti-GBM/ANCA vasculitis
- monoclonal antibodies → lupus nephritis.

Small vessel vasculitis

ANCA-associated vasculitis (AAV) classically presents at an older age (>60yrs) and accounts for 20% of biopsy findings >80yrs.

- Ask about lethargy, fever, myalgia, anorexia
- Ask about respiratory symptoms and investigate for pulmonary haemorrhage.

Diagnosis:

Clinical + ANCA + biopsy → rapidly progressive GN without immune deposits ('pauci-immune').

Treatment:

High-dose glucocorticoids plus cyclophosphamide or rituximab.

Plasma exchange if presents with renal failure or pulmonary haemorrhage.

ANCA ⊕ Vasculitis (pauci-immune, minimal staining) ~40–45% of total						
Pathogen: ? bacterial infxn, drugs (hydral, allopurinol, contam cocaine) (CJASN 2011;6:2799)						
Disease	Gran	Renal	Pulm	Asthma	ANCA Type ^a	ANCA ⊕
Granulomatosis with polyangiitis ^b	⊕	80%	90% (+ ENT)	—	anti-PR3 (c-ANCA)	90%
Microscopic polyangiitis	—	90%	50%	—	anti-MPO (p-ANCA)	70%
Eosinophilic gran with polyangiitis ^c	⊕	45%	70%	⊕	anti-MPO (p-ANCA)	50%

Nephritic vs Nephrotic

	Nephrotic Syndrome	Nephritic Syndrome
Diagnosis	- Nephrotic range proteinuria (>3 g /24 hr Or PCR > 300 mg/mmol Or ACR >200 mg/mmol) - Oedema - Hypoalbuminaemia (<3.5 g/dL)	- Glomerular Haematuria - Oliguria Hypertension - Oedema GFR: moderate-severe ↓
Additional features	Hyperlipidemia (hepatic lipoprotein synthesis in response to low oncotic pressure.) Increase risk of thrombosis (Loss of antithrombin-III, proteins C and S and an associated rise in fibrinogen) Susceptibility to infection: ↓serum IgG, ↓complement activity, and ↓T cell function BP: usually normal-mild ↑ GFR: usually normal-mild ↓	PRGN is severe spectrum
Causes	Membranous GN Minimal change FSGS MPGN (mesangiocapillary GN) Secondary : Diabetes, SLE (class V nephritis), Amyloid	IgA nephropathy MPGN (Mesangiocapillary GN) Secondary: Post streptococcal, Vasculitis, SLE (other classes of nephritis), Anti-GBM disease, Cryoglobulinaemia

Kidney Biopsy

- **Indications**
 1. glomerular hematuria
 2. severely increased albuminuria
 3. acute or CKD of unclear origin
 4. kidney transplant dysfunction
- **Complications**
 1. Bleeding
 2. Trauma.
 3. A-V fistula.
 4. Infection.
- **Contraindications**
 1. bleeding diatheses
 2. severe anemia
 3. UTI, Hydronephrosis.
 4. uncontrolled hypertension
 5. renal tumor
 6. Atrophic kidneys.
 7. solitary kidney (except renal transplant)

Etiology of Nephrotic syndrome

Due to primary renal disease or secondary to a systemic disorder.

- Primary renal disease: Minimal change disease, membranous nephropathy (may be associated with underlying inflammation/malignancy), focal segmental glomerulosclerosis (FSGS), membranoproliferative GN.
- Secondary causes: DM, lupus nephritis, myeloma, amyloid, pre-eclampsia.

Pathophysiology

- Podocyte pathology: abnormal function in minimal change disease/ immune-mediated damage in membranous nephropathy/ and podocyte injury or death in FSGS.
- Pathology in the GBM/endothelial cell: membranoproliferative GN.

Presentation

- Generalized, pitting edema, which can be rapid and severe.
- History: Ask about systemic symptoms, eg joint, skin.

Management

1. Reduce edema
2. Treat underlying cause
3. Reduce proteinuria
4. Treat complications:
 - Thromboembolism: Hypercoagulable due to loss of anti-thrombins in the form of proteinuria and increased clotting factors → Risk of VTE including DVT/PE + renal vein thrombosis (loin pain, haematuria, increased LDH, AKI if the thrombosis is bilateral).
 - Treat with LMW heparin and warfarin. consider prophylaxis when albumin becomes <20g/L.
 - Infection: Urine losses of immunoglobulins and immune mediators → increase risk of urinary, respiratory, and CNS infection.
 - Hyperlipidemia
 - Give statins

NEPHROTIC

1ry causes:

- Minimal change
- Focal segmental glomerulosclerosis
- Membranous nephropathy
- membranoproliferative

2ry causes:

- Diabetic nephropathy
- Lupus nephritis
- Myeloma
- Amyloid
- Pre-eclampsia

NEPHRITIC

- IgA Nephropathy
- Henoch-scholein Purpura
- Post-streptococcal GN
- Goodpastures (anti-GBM disease)
- Rapidly progressive GN

Lupus nephritis:

- Affects 40-60% of SLE patients
- Can give any degree of renal involvement from minimal change → CKD.
- Hypertension occurs stage 3+
- Most patients present at stage 4
- Biopsy is the most accurate test and helps stage the disease to help determine the prognosis.
- **Treatment:**
 - Glucocorticoids and Cyclophosphamide (stage 3+).
 - BP control with ACEi/ARBs

	Class	Pathology	Clinical significance
I	Minimal change LN	Immune deposits but normal on L/M	Asymptomatic
II	Mesangial LN	Mesangial hypercellularity and matrix expansion	Mild renal disease microscopic haematuria and/or proteinuria
III	Focal Proliferative LN	Involving <50% of glomeruli, Subendothelial deposits	haematuria and proteinuria in ALL May be NS, HTN, ↑ creatinine
IV	Diffuse Proliferative LN	Involving >50% of glomeruli, Subendothelial deposits	Most common and most severe form of LN haematuria and proteinuria in ALL NS, HTN, ↑ creatinine are common
V	Membranous LN	Membranous GN	Nephrotic syndrome
VI	Sclerosing LN	≥90% globally sclerosed glomeruli without residual activity	Progressive CKD

Renal papillary Necrosis

Sloughing of the papillary → shedding → obstruction of uteric outlet

- Hematuria
- Acute loin pain

Causes:

- DM
- Sickle cell disease
- NSAIDs
- Pyelonephritis
- Accelerated HTN

Diagnosis: Non-contrast CT → papillary blunting and necrosis.

Renal vein thrombosis

- **Causes:** Acute → Gastroenteritis/ acute pyelonephritis
Chronic → Amyloidosis / nephrotic syndrome (esp. Membranous GN)
- **Presentation:** Asymptomatic/ flank pain / Macroscopic hematuria/ unexplained AKI (sudden increase in creatinine)/ sudden Proteinuria.

Renal Artery Stenosis

1. Atherosclerosis → M.C.C → old male with vascular problems.
2. Fibromuscular dysplasia → young female with hypertension.

Presentation: Resistant HTN/ increased creatinine after ACEis / flash pulm. Edema → Rx: Spironolactone / abdominal bruit/ Asymmetry in kidney size on U/S.

Diagnosis: MRA best imaging technique

Treatment: 1) Antihypertensive regimens 2) Angioplasty/ stent 3) Revascularization surgery

Medical Rx preferred because of risk of Cholesterol embolisms in stenting Atherosclerotic pts.

Cholesterol Embolic Syndrome: AKI, Hypertension, distal ischemia, acute multisystemic dysfunction after invasive arterial procedure/ thrombolytic therapy

Renal Tubular Acidosis

Renal tubular

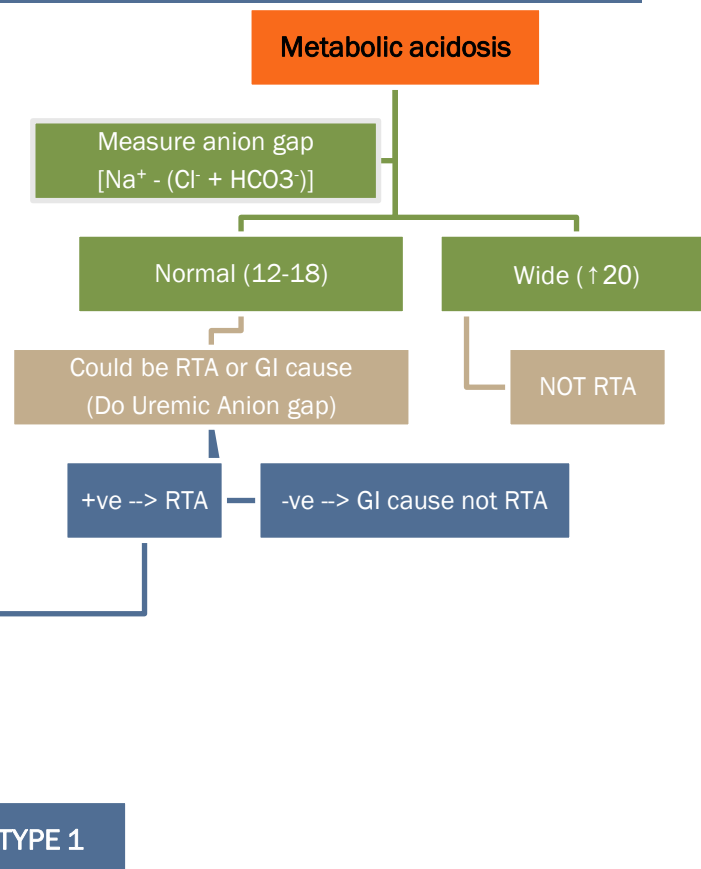
acidosis (RTA) is a disorder of the renal tubules that leads to a non-anion gap hyperchloremic metabolic acidosis.

- Glomerular function is normal
- It is characterized by a decrease in the H^+ excreted in the urine, leading to acidemia and urine alkalosis.
- There are three types of RTA (types 1, 2, and 4). (Type 3 RTA is a term that is no longer used.)

Type	Characteristics	Associations
1 (Distal) 'Stones'	Can't secrete H^+ Alkaline urine Hypokalemia Nephrolithiasis & Nephrocalcinosis <u>OCCUR</u>	Sjogren's Syn. SLE Urinary obstruction
2 (Proximal) 'Bones'	Can't reabsorb HCO_3^- → Increased bicarb. excretion Acidic urine Hypokalemia <u>NO</u> Nephrolithiasis & Nephrocalcinosis	Multiple Myeloma Acetazolamide Fanconi Syn. Osteomalacia/ rickets
3 (Mixed)	AR → Carbonic Anhydrase 2 deficiency (RARE)	
4 (Hyperaldosteronism) 'Low Aldosterone'	Decreased Na^+ absorption and H^+ and K^+ secretion in distal tubules Acidic urine Hyperkalemia Nephrolithiasis & Nephrocalcinosis → RARE	Spirolactone Trimethoprim Hypoaldosteronism

Fanconi Syndrome

- Hereditary or acquired
- Proximal tubule dysfunction → defective transport of glucose, amino acids, sodium, potassium, phosphate, uric acid, and bicarbonate.
- Presentation: glucosuria, phosphaturia (osteomalacia, osteoporosis, and pathologic fractures), proteinuria, polyuria, dehydration, type 2 RTA, hypercalciuria, and hypokalemia.
- Treat with phosphate, potassium, alkali and salt supplementation, as well as adequate hydration.



Autosomal Dominant Polycystic Kidney Disease

(ADPKD) is the most common inherited cause of kidney disease. It is an autosomal dominant disorder affecting 1 in 1,000 Caucasians and accounting for approximately 8% of cases of end-stage renal disease (ESRD).

➤ Typically presents ages of 30-50.

Two disease have been identified, PKD1 and PKD2.

ADPKD presents with:

- Pain → cyst rupture/ infection
- Hematuria → cyst rupture → poor prognosis if gross hematuria.
- Infection
- Hypertension → earliest manifestation
- Kidney stones

ADPKD TYPE 1	ADPKD TYPE 2
85% OF CASES	15% OF CASES
Chromosome 16	Chromosome 4
ESFR → 50yrs	ESRF → 70yrs

Screening for cerebral aneurysms should only be carried out in high risk patients:

- Previous rupture of aneurysm
- Concerning neurological symptoms (for example, severe headache)
- Positive family history of hemorrhagic stroke or aneurysm.

MRA → to screen for cerebral aneurysms.

Renal complications

1. CKD → ↑PO₄ ↓Ca

BUT (N/↑) hemoglobin due to ↑ erythropoietin secretion → Polycythemia

2. Renal cell carcinoma with lung metastasis → Cannon ball appearance on CXR

Associations:

Cardiovascular system:

Mitral valve prolapse (25%) → M.C → (needs echo screening).

Mitral/tricuspid incompetence, aortic root dilation, aortic dissection

GIT

Colonic diverticula (with any related symptoms, screen by barium enema)

Liver cysts

cysts in other organs:

Pancreas, spleen; very rarely: thyroid, esophagus, ovaries.

CNS

Berry aneurysms → subarachnoid Hemorrhage/ or Asymptomatic

Renal biopsy is contraindicated due to a high risk of hemorrhage into a cyst

Prognosis

Gradual deterioration in renal function → 50% of patients require dialysis by 60 years.

Investigations:

- Ultrasound → Very sensitive
 - <30 yrs → 2 unilateral/ bilateral cysts
 - 30-59 yrs → 2 cysts in each kidney
 - >60 yrs → 4 cysts in each kidney

CT abdomen and thorax
for renal cell carcinoma
+ lung metastasis

Treatment

- High fluid intake (to prevent the formation of renal stones or blood clots)
- Non-NSAID-based analgesia → IV fluids, paracetamol and codeine.
- Hypertension → ACE inhibitors or ARBs → also reduces cyst formation in ADPKD
- Aliskiren (direct renin inhibitor) → reducing new cysts.
- Tolvaptan (selective vasopressin antagonist) → delay disease progression.
- UTI should be treated ———ciprofloxacin, trimethoprim- sulphamethoxazole has the best penetration into cyst fluid.
- End-stage renal disease → Transplantation

Renal Stones

Renal stones (calculi) consist of crystal aggregates. Stones form in collecting ducts and may be deposited anywhere from the renal pelvis to the urethra.

Types

- | | |
|--------------------------------------|---------------------------|
| – Calcium oxalate (75%) | – Calcium phosphate (15%) |
| – Magnesium ammonium phosphate (15%) | – cysteine (1%) |
| – Uric acid | – Mixed stone |

Presentation

Could be asymptomatic.

- | | |
|---|--|
| 1. Pain → Renal Colic / Flank pain | 4. hematuria |
| 2. Nausea & vomiting | 5. proteinuria |
| 3. Infection → UTI/ Pyelonephritis/
pyonephrosis | 6. sterile pyuria |
| | 7. anuria / urinary tract obstruction Sx |

Clinical course:

- If a stone is >1 cm, it is unlikely to pass spontaneously.
- Stones <0.5 cm 90-95% pass spontaneously
- Recurrence is common → up to 50% of the patients have recurrences within 10 years.

Investigations

- CBC, U&E, Ca⁺, PO₄, glucose, bicarbonate, urate.
- Urine dipstick: Usually +ve for blood (90%).
- Urine for C&S / pH / 24h urine for: calcium, oxalate, urate, citrate, sodium, creatinine
- Stone biochemistry (sieve urine & send stone).

Imaging

- Non-contrast CT is investigation of choice for imaging stones (99% visible)
 - Early detection early detection of Hydronephrosis
 - Helps exclude DD of acute abdomen.
- 80% of stones are visible on KUB X-Ray (kidneys + ureters + bladder).
- Ultrasound an alternative for Hydronephrosis or Hydroureter.

Type	Causative factors	Treatment	Appearance / on X-Ray
Ca oxalate	Idiopathic Metabolic Chron's disease Ethyl glycol poisoning Pyridoxine deficiency (2ry hyperoxaluria)	– High fluid intake – Dietary oxalate restriction – Citrate → Inhibits Ca crystallization – Pyridoxine – AVOID severe calcium restriction ↑ precipitation of oxalate.	Spiky, radio-opaque
Ca phosphate	Idiopathic metabolic	– High fluid intake – Thiazide diuretics – ↓ protein and salt diet – AVOID severe calcium restriction ↑ precipitation of oxalate → oxalate stones	Smooth, may be large, radioopaque
Magnesium ammonium Phosphate (STRUVITE)	Recurrent UTIs due to urease-producing organisms (Proteus , Klebsiella , Enterobacter)	– High fluid intake – Treat infection	Large, horny, 'staghorn', radioopaque
Urate	Hyperuricaemia Hyperuricosuria Due to ↑ cell turnover (Myeloproliferative disorders)	– High fluid intake – Allopurinol – If tumor-lysis synd. → rasburicase – Alkalization of urine	Smooth, brown, radiolucent
cysteine	Renal tubular defects Cystinuria	– Alkalization of urine – High fluid intake – D-penicillamine – CAPTOPRIL (binds to cysteine and ↑ its solubility) – Tiopronin (Cystiene chalator)	Yellow, crystalline, semi-opaque

Management of Renal Colic
 Diclofenac oral/IM
 Morphine IV
 Alpha blockers → Tamsulosin

Causes of hypercalcemia

1. Sarcoidosis
2. Vitamin D
3. 1ry hyperparathyroidism

